

Toxicology Research Laboratory

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at Chicago

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Contract No.: DAMD17-92-C2001
Task Order No.: UIC-5B
UIC/TRL Study No.: 098

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Title Page

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Volume 3 of 3
Draft Report for Task Order No. UIC-5B
THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

Sponsor: US Army Medical Materiel
Development Activity

Test Article: WR238605

Contract No.: DAMD17-92-C-2001

Study Director

Barry S. Levine, D.Sc., D.A.B.T.

In-Life Phase Completed On

June 18, 1993

Performing Laboratory

TOXICOLOGY RESEARCH LABORATORY (TRL)
University of Illinois at Chicago (UIC)
Department of Pharmacology
1940 W. Taylor St.
Chicago, IL 60612-7353

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| | | | Toxicology Antimalarial | | |
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| <p>This study evaluated the toxicity of WR238605 in rats following thirteen weeks of daily oral (gavage) administration. A thirteen week recovery period was included for all groups. Dose levels studied were 0 (vehicle control), 0.5, 6 and 18 mg base/kg/day. The primary toxic affects were seen in the RBCs, lungs, and liver. Significant methemoglobin production was observed in mid and high dose animals, but was reversible. Microscopic lesions in the spleen, kidney, and bone marrow were secondary to mild hemolytic anemia. Toxicity again was limited to the two highest dose levels. Decreased food consumption, decreased body weight gains, methemoglobin production and mild anemia were observed at the mid and high dose levels, but were readily reversible after treatment cessation. Increases in serum ALT, AST, and/or LDH and decreased A/G ratios in high dose animals and possibly mid dose males suggested mild hepatotoxicity, however histopathologic lesions were not seen. Leukocytosis possibly secondary to stress and consisting of increased number of lymphocytes, mature neutrophils, and/or monocytes was seen in the treatment period at the two highest dose levels and was reversible after cessation of treatment. Because the aforementioned toxic responses were limited to mid and high dose animals, a no-adverse effect level of WR238605 was assessed to be 0.5 mg base/kg/day.</p> | | | | | |
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VOLUME 3

APPENDICES (Contd.)

| | | |
|----|--|------|
| 7 | Individual Hematology Data | 7-1 |
| 8 | Ophthalmology Report | 8-1 |
| 9 | Individual Organ Weights | 9-1 |
| 10 | Pathology Report | 10-1 |
| 11 | Pre-test Clinical Pathology Data | 11-1 |
| 12 | Protocol and Protocol Amendments | 12-1 |
| 13 | Study Deviations | 13-1 |

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APPENDIX 7

Individual Hematology Data

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: 098
ABBR: RBC

SEX: MALE
UNITS: 10⁶/cm³

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 801 | 7.64 | 7.98 | 8.57 | 8.56 | 8.42 | 9.04 | 8.40 |
| 802 | 7.47 | 8.08 | 8.47 | 8.48 | 8.49 | 8.68 | 8.83 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 7.89 | 8.28 | 8.49 | 8.39 | 8.73 | 9.09 | 8.90 |
| 807 | 7.34 | 7.75 | 8.28 | 8.34 | 8.14 | 8.33 | 8.32 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 7.56 | 8.02 | 8.07 | 8.61 | 8.13 | 8.43 | 8.23 |
| 810 | 6.68 | 7.00 | 7.58 | 8.04 | 7.84 | 8.68 | 7.22 |
| 811 | 7.04 | 7.78 | 7.84 | 8.15 | 8.94 | 8.80 | 8.22 |
| 812 | -- | -- | -- | 7.77 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 7.43 | 7.56 | 8.32 | 7.94 | 7.84 | 8.44 | 8.27 |
| 815 | 6.77 | 7.19 | 7.65 | 7.28 | 7.89 | 7.71 | 7.83 |
| 816 | 7.16 | 7.13 | 7.64 | 7.66 | 7.54 | 8.28 | 7.68 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 7.30 | 7.68 | 8.09 | 8.11 | 8.20 | 8.55 | 8.19 |
| SD | 0.385 | 0.442 | 0.386 | 0.420 | 0.442 | 0.406 | 0.507 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|-------|-------|-------|-------|-------|-------|-------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 7.32 | 8.13 | 8.20 | 8.68 | 8.06 | 8.28 | 8.55 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 7.47 | 7.61 | 8.00 | 8.28 | 7.80 | 8.30 | 8.27 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 7.27 | 7.40 | 8.23 | 8.65 | 8.21 | 8.56 | 8.65 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 7.69 | 8.29 | 8.27 | 8.57 | 8.00 | 9.19 | 8.64 |
| 851 | 7.07 | 7.64 | 8.15 | 6.61 | 7.89 | 8.15 | 8.15 |
| 852 | 7.30 | 7.30 | 7.83 | 7.79 | 7.76 | 7.92 | 7.92 |
| 853 | 6.79 | 7.05 | 8.15 | 8.15 | 8.20 | 8.64 | 8.35 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 7.21 | 7.71 | 8.20 | 8.51 | 8.09 | 8.83 | 8.42 |
| 859 | 7.28 | 7.54 | 8.50 | 8.21 | 8.09 | 8.05 | 7.98 |
| 860 | 6.71 | 6.68 | 7.55 | 7.84 | 7.85 | 7.93 | 7.79 |
| MEAN | 7.21 | 7.54 | 8.11 | 8.13 | 8.00 | 8.39 | 8.27 |
| SD | 0.293 | 0.473 | 0.262 | 0.619 | 0.162 | 0.415 | 0.305 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: 098
ABBR: RBC

SEX: MALE
UNITS: 10⁶/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 7.21 | 7.36 | 7.92 | 8.61 | 8.23 | 8.78 | 7.68 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 7.26 | 7.35 | 7.64 | -- | 7.85 | 9.52 | 8.33 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 6.97 | 7.40 | 7.59 | 7.78 | 8.01 | 9.11 | 8.68 |
| 890 | 6.95 | 7.26 | 7.84 | 7.34 | 7.97 | 9.09 | 8.56 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 7.14 | 6.94 | 7.40 | 7.95 | 6.71 | 8.75 | 8.87 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 6.47 | 7.06 | 7.72 | 8.35 | 8.11 | 9.11 | 8.15 |
| 896 | 7.75 | 7.40 | 8.21 | 8.55 | 8.61 | 8.97 | 8.83 |
| 897 | 7.21 | 7.18 | 8.20 | 8.00 | 8.40 | 8.19 | 8.54 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 8.29 | 7.82 | 7.21 | 7.66 | 8.02 | 8.57 | 8.46 |
| 900 | 6.94 | 7.20 | 8.04 | 7.75 | 8.82 | 9.32 | 8.39 |
| MEAN | 7.22 | 7.30 | 7.78 | 8.00 | 8.07 | 8.94 | 8.45 |
| SD | 0.496 | 0.238 | 0.330 | 0.427 | 0.568 | 0.383 | 0.349 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|---------------------------------|-------|-------|-------|-------|-------|-------|-------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 7.72 | 8.54 | 8.71 | 8.85 |
| 923 | 6.23 | 7.20 | 7.50 | 8.37 | 8.02 | 8.98 | 8.43 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 7.35 | 7.23 | 8.49 | 7.82 | 8.29 | 8.96 | 8.20 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 7.20 | 8.33 | 8.07 | 8.04 | 8.25 | 9.36 | 9.16 |
| 930 | 5.92 | 6.25 | 7.41 | 8.18 | 7.94 | 8.51 | 7.87 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 7.01 | 7.55 | 8.01 | 7.42 | 8.36 | 8.50 |
| 933 | 6.32 | 7.15 | 7.95 | 7.99 | 8.75 | 9.90 | 9.33 |
| 934 | 6.44 | 7.12 | 7.98 | -- | -- | -- | -- |
| 935 | 6.02 | 7.16 | 7.18 | 7.45 | 7.56 | 8.41 | 7.66 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 7.30 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 6.26 | 7.00 | 7.95 | 7.26 | 7.11 | 8.04 | 7.92 |
| 940 | 6.51 | 7.15 | 7.54 | 7.73 | 7.63 | 8.65 | 8.30 |
| MEAN | 6.56 | 7.16 | 7.76 | 7.86 | 7.95 | 8.79 | 8.42 |
| SD | 0.533 | 0.500 | 0.390 | 0.333 | 0.521 | 0.539 | 0.554 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

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INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: 098
ABBR: THGB

SEX: MALE
UNITS: g/dL

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 14.9 | 14.7 | 15.0 | 16.2 | 15.5 | 15.8 | 14.5 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 15.3 | 15.6 | 15.5 | -- | 15.4 | 17.6 | 16.2 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 15.1 | 15.6 | 14.9 | 15.3 | 15.2 | 16.6 | 15.9 |
| 890 | 14.8 | 15.2 | 15.2 | 14.5 | 14.9 | 16.2 | 15.6 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 15.4 | 14.9 | 14.6 | 15.4 | 14.2 | 16.1 | 16.3 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 14.2 | 14.5 | 14.8 | 15.3 | 14.8 | 16.1 | 14.8 |
| 896 | 16.0 | 15.4 | 16.0 | 16.2 | 16.4 | 17.1 | 16.5 |
| 897 | 15.5 | 14.8 | 15.8 | 14.8 | 15.7 | 14.7 | 15.7 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 17.0 | 16.4 | 14.5 | 15.1 | 15.6 | 15.5 | 16.0 |
| 900 | 15.5 | 16.0 | 16.0 | 14.8 | 16.8 | 16.6 | 16.0 |
| MEAN | 15.4 | 15.3 | 15.2 | 15.3 | 15.5 | 16.2 | 15.8 |
| SD | 0.75 | 0.61 | 0.56 | 0.59 | 0.76 | 0.82 | 0.64 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 14.6 | 16.1 | 15.8 | 16.0 |
| 923 | 13.8 | 14.9 | 13.7 | 14.8 | 14.9 | 16.5 | 16.0 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 14.9 | 14.2 | 15.2 | 13.8 | 15.4 | 15.9 | 15.1 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 14.2 | 15.4 | 13.6 | 13.9 | 14.9 | 16.8 | 16.8 |
| 930 | 12.9 | 13.1 | 14.8 | 15.1 | 15.6 | 15.9 | 15.2 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 14.1 | 15.4 | 15.4 | 15.2 | 16.0 | 16.0 |
| 933 | 12.5 | 13.8 | 13.9 | 13.1 | 14.6 | 16.2 | 16.0 |
| 934 | 14.3 | 15.3 | 15.4 | -- | -- | -- | -- |
| 935 | 13.2 | 14.9 | 13.5 | 14.5 | 15.0 | 16.3 | 15.5 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 14.5 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 13.2 | 14.3 | 14.9 | 13.3 | 14.1 | 15.2 | 15.0 |
| 940 | 13.1 | 13.6 | 14.0 | 13.3 | 13.8 | 15.3 | 15.2 |
| MEAN | 13.7 | 14.4 | 14.4 | 14.2 | 15.0 | 16.0 | 15.7 |
| SD | 0.79 | 0.75 | 0.77 | 0.81 | 0.68 | 0.50 | 0.57 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: 098
ABBR: HCT

SEX: MALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 801 | 44.4 | 45.5 | 45.2 | 42.5 | 42.4 | 44.9 | 41.0 |
| 802 | 44.9 | 47.6 | 46.2 | 42.9 | 43.6 | 43.7 | 44.2 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 46.6 | 47.3 | 44.6 | 42.5 | 45.4 | 45.8 | 45.1 |
| 807 | 46.0 | 47.7 | 48.1 | 47.1 | 47.0 | 48.0 | 46.8 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 46.3 | 47.8 | 45.1 | 46.3 | 44.6 | 45.3 | 44.6 |
| 810 | 40.8 | 41.4 | 40.3 | 40.7 | 40.6 | 43.9 | 35.6 |
| 811 | 42.9 | 46.1 | 43.0 | 43.0 | 47.7 | 45.8 | 42.3 |
| 812 | -- | -- | -- | 40.4 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 47.4 | 46.6 | 49.2 | 45.7 | 45.6 | 48.4 | 46.6 |
| 815 | 43.6 | 45.2 | 44.1 | 40.5 | 43.9 | 42.2 | 41.9 |
| 816 | 43.8 | 42.7 | 42.6 | 41.3 | 40.8 | 43.4 | 39.6 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 44.7 | 45.8 | 44.8 | 43.0 | 44.2 | 45.1 | 42.8 |
| SD | 1.99 | 2.19 | 2.61 | 2.38 | 2.40 | 1.97 | 3.45 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 44.5 | 47.0 | 44.2 | 45.5 | 43.7 | 44.2 | 44.5 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 46.0 | 46.0 | 45.2 | 45.5 | 43.0 | 45.4 | 44.4 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 47.2 | 46.6 | 49.2 | 50.1 | 47.9 | 49.2 | 49.1 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 45.4 | 48.0 | 45.8 | 45.2 | 43.1 | 47.9 | 44.8 |
| 851 | 43.6 | 45.9 | 46.5 | 36.5 | 43.2 | 44.3 | 44.2 |
| 852 | 46.0 | 45.0 | 44.8 | 43.4 | 43.1 | 42.9 | 42.6 |
| 853 | 41.6 | 43.1 | 45.9 | 44.3 | 44.8 | 46.2 | 43.9 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 43.5 | 45.4 | 45.3 | 45.2 | 43.0 | 46.4 | 43.1 |
| 859 | 43.0 | 43.1 | 45.8 | 43.6 | 43.6 | 43.1 | 42.0 |
| 860 | 42.2 | 40.5 | 42.8 | 42.5 | 43.1 | 42.6 | 41.2 |
| MEAN | 44.3 | 45.1 | 45.6 | 44.2 | 43.9 | 45.2 | 44.0 |
| SD | 1.82 | 2.24 | 1.65 | 3.39 | 1.53 | 2.21 | 2.15 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: 098
ABBR: HCT

SEX: MALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 42.2 | 41.1 | 42.4 | 44.4 | 43.5 | 44.2 | 39.8 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 43.8 | 44.4 | 42.2 | -- | 43.0 | 49.4 | 44.1 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 42.2 | 43.4 | 41.7 | 41.9 | 42.9 | 46.5 | 45.0 |
| 890 | 42.6 | 43.1 | 43.0 | 38.8 | 41.7 | 45.4 | 43.0 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 44.3 | 42.7 | 42.0 | 42.9 | 36.6 | 44.6 | 44.8 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 41.3 | 42.1 | 42.2 | 43.4 | 42.3 | 45.6 | 41.2 |
| 896 | 47.1 | 44.1 | 45.5 | 45.3 | 46.7 | 47.4 | 47.3 |
| 897 | 44.1 | 42.6 | 44.6 | 41.2 | 43.9 | 40.9 | 43.2 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 49.6 | 47.5 | 43.0 | 41.1 | 44.6 | 43.8 | 44.6 |
| 900 | 44.0 | 44.5 | 44.8 | 41.8 | 47.4 | 48.0 | 43.5 |
| MEAN | 44.1 | 43.6 | 43.1 | 42.3 | 43.3 | 45.6 | 43.7 |
| SD | 2.51 | 1.75 | 1.34 | 1.95 | 2.97 | 2.42 | 2.08 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 40.7 | 44.8 | 43.6 | 44.6 |
| 923 | 38.9 | 43.3 | 39.7 | 41.9 | 42.7 | 47.1 | 44.8 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 43.1 | 41.0 | 43.7 | 39.3 | 43.0 | 44.4 | 41.7 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 41.6 | 44.9 | 40.3 | 39.6 | 42.5 | 47.5 | 47.0 |
| 930 | 37.4 | 38.9 | 42.0 | 43.3 | 45.0 | 44.6 | 42.5 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 42.2 | 43.9 | 45.5 | 43.2 | 44.2 | 44.7 |
| 933 | 36.0 | 39.5 | 38.2 | 36.8 | 40.7 | 45.3 | 43.9 |
| 934 | 39.5 | 42.9 | 43.4 | -- | -- | -- | -- |
| 935 | 38.2 | 43.2 | 39.6 | 40.1 | 43.4 | 45.0 | 42.9 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 42.6 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 38.0 | 41.2 | 42.5 | 39.0 | 38.7 | 41.5 | 41.3 |
| 940 | 36.8 | 40.7 | 40.0 | 38.4 | 39.8 | 42.4 | 42.2 |
| MEAN | 39.2 | 41.8 | 41.3 | 40.5 | 42.4 | 44.6 | 43.6 |
| SD | 2.46 | 1.86 | 2.02 | 2.53 | 2.05 | 1.85 | 1.76 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: 098
ABBR: MCV

SEX: MALE
UNITS: fL

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 801 | 58.1 | 57.0 | 52.7 | 49.6 | 50.4 | 49.7 | 48.8 |
| 802 | 60.1 | 58.9 | 54.5 | 50.6 | 51.4 | 50.3 | 50.1 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 59.1 | 57.1 | 52.5 | 50.7 | 52.0 | 50.4 | 50.7 |
| 807 | 62.7 | 61.5 | 58.1 | 56.5 | 57.7 | 57.6 | 56.3 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 61.2 | 59.6 | 55.9 | 53.8 | 54.9 | 53.7 | 54.2 |
| 810 | 61.1 | 59.1 | 53.2 | 50.6 | 51.8 | 50.6 | 49.3 |
| 811 | 60.9 | 59.3 | 54.8 | 52.8 | 53.4 | 52.0 | 51.5 |
| 812 | -- | -- | -- | 52.0 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 63.8 | 61.6 | 59.1 | 57.6 | 58.2 | 57.3 | 56.3 |
| 815 | 64.4 | 62.9 | 57.6 | 55.6 | 55.6 | 54.7 | 53.5 |
| 816 | 61.2 | 59.9 | 55.8 | 53.9 | 54.1 | 52.4 | 51.6 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 61.3 | 59.7 | 55.4 | 53.1 | 54.0 | 52.9 | 52.2 |
| SD | 1.96 | 1.90 | 2.31 | 2.66 | 2.66 | 2.89 | 2.72 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 60.8 | 57.8 | 53.9 | 52.4 | 54.2 | 53.4 | 52.0 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 61.6 | 60.4 | 56.5 | 55.0 | 55.1 | 54.7 | 53.7 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 64.9 | 63.0 | 59.8 | 57.9 | 58.3 | 57.5 | 56.8 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 59.0 | 57.9 | 55.4 | 52.7 | 53.9 | 52.1 | 51.9 |
| 851 | 61.7 | 60.1 | 57.1 | 55.2 | 54.8 | 54.4 | 54.2 |
| 852 | 63.0 | 61.6 | 57.2 | 55.7 | 55.5 | 54.2 | 53.8 |
| 853 | 61.3 | 61.1 | 56.3 | 54.4 | 54.6 | 53.5 | 52.6 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 60.3 | 58.9 | 55.2 | 53.1 | 53.2 | 52.5 | 51.2 |
| 859 | 59.1 | 57.2 | 53.9 | 53.1 | 53.9 | 53.5 | 52.6 |
| 860 | 62.9 | 60.6 | 56.7 | 54.2 | 54.9 | 53.7 | 52.9 |
| MEAN | 61.5 | 59.9 | 56.2 | 54.4 | 54.8 | 54.0 | 53.2 |
| SD | 1.82 | 1.87 | 1.74 | 1.67 | 1.39 | 1.48 | 1.58 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: 098
ABBR: MCV

SEX: MALE
UNITS: fL

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 58.5 | 55.8 | 53.5 | 51.6 | 52.9 | 50.3 | 51.8 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 60.3 | 60.4 | 55.2 | -- | 54.8 | 51.9 | 52.9 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 60.5 | 58.6 | 54.9 | 53.9 | 53.6 | 51.0 | 51.8 |
| 890 | 61.3 | 59.4 | 54.8 | 52.9 | 52.3 | 49.9 | 50.2 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 62.0 | 61.5 | 56.8 | 54.0 | 54.5 | 51.0 | 50.5 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 63.8 | 59.6 | 54.7 | 52.0 | 52.2 | 50.1 | 50.6 |
| 896 | 60.8 | 59.6 | 55.4 | 53.0 | 54.2 | 52.8 | 53.6 |
| 897 | 61.2 | 59.3 | 54.4 | 51.5 | 52.3 | 49.9 | 50.6 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 59.8 | 60.7 | 59.6 | 53.7 | 55.6 | 51.1 | 52.7 |
| 900 | 63.4 | 61.8 | 55.7 | 53.9 | 53.7 | 51.5 | 51.8 |
| MEAN | 61.2 | 59.7 | 55.5 | 52.9 | 53.6 | 51.0 | 51.7 |
| SD | 1.60 | 1.69 | 1.68 | 1.02 | 1.18 | 0.94 | 1.16 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 52.7 | 52.5 | 50.1 | 50.4 |
| 923 | 62.4 | 60.1 | 52.9 | 50.1 | 53.2 | 52.4 | 53.1 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 58.6 | 56.7 | 51.5 | 50.3 | 51.9 | 49.6 | 50.9 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 57.8 | 53.9 | 49.9 | 49.3 | 51.5 | 50.7 | 51.3 |
| 930 | 63.2 | 62.2 | 56.7 | 52.9 | 56.7 | 52.4 | 54.0 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 60.2 | 58.1 | 56.8 | 58.2 | 52.9 | 52.6 |
| 933 | 57.0 | 55.2 | 48.1 | 46.1 | 46.5 | 45.8 | 47.1 |
| 934 | 61.3 | 60.3 | 54.4 | -- | -- | -- | -- |
| 935 | 63.5 | 60.3 | 55.2 | 53.8 | 57.4 | 53.5 | 56.0 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 58.4 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 60.7 | 58.9 | 53.5 | 53.7 | 54.4 | 51.6 | 52.1 |
| 940 | 56.5 | 56.9 | 53.1 | 49.7 | 52.2 | 49.0 | 50.8 |
| MEAN | 59.9 | 58.5 | 53.3 | 51.5 | 53.5 | 50.8 | 51.8 |
| SD | 2.60 | 2.66 | 3.01 | 3.02 | 3.44 | 2.30 | 2.38 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 098
ABBR: TMCH

SEX: MALE
UNITS: pg

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|-----|------|------|------|------|------|------|------|
| 801 | 20.5 | 19.9 | 19.0 | 18.0 | 18.5 | 17.8 | 17.6 |
| 802 | 21.0 | 20.9 | 20.1 | 18.5 | 18.7 | 18.1 | 17.8 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 20.9 | 20.4 | 19.1 | 18.8 | 18.8 | 18.6 | 18.0 |
| 807 | 22.2 | 21.9 | 21.3 | 21.0 | 21.5 | 20.6 | 20.6 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 21.6 | 21.1 | 21.3 | 19.5 | 20.3 | 19.6 | 19.8 |
| 810 | 21.4 | 21.0 | 19.1 | 18.4 | 18.8 | 18.0 | 20.1 |
| 811 | 21.6 | 21.0 | 19.9 | 19.8 | 19.0 | 18.6 | 19.1 |
| 812 | -- | -- | -- | 21.0 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 21.4 | 20.8 | 20.9 | 20.2 | 21.4 | 19.7 | 19.6 |
| 815 | 22.7 | 22.7 | 20.7 | 20.6 | 20.5 | 19.8 | 19.3 |
| 816 | 21.1 | 21.7 | 20.0 | 19.8 | 19.6 | 18.7 | 19.1 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 21.4 | 21.1 | 20.1 | 19.6 | 19.7 | 19.0 | 19.1 |
| SD | 0.64 | 0.79 | 0.89 | 1.06 | 1.14 | 0.92 | 1.01 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|-----|------|------|------|------|------|------|------|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 21.2 | 20.0 | 19.4 | 19.2 | 19.5 | 19.2 | 18.7 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 21.4 | 21.2 | 21.0 | 19.8 | 20.4 | 18.8 | 19.6 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 21.9 | 21.9 | 21.5 | 20.6 | 20.6 | 20.1 | 19.8 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 21.2 | 20.3 | 20.1 | 19.0 | 19.5 | 18.6 | 18.9 |
| 851 | 21.5 | 21.5 | 20.5 | 11.8 | 19.9 | 19.8 | 20.1 |
| 852 | 21.6 | 21.6 | 21.1 | 20.3 | 20.1 | 19.8 | 19.7 |
| 853 | 20.8 | 21.1 | 20.1 | 19.4 | 19.5 | 19.0 | 18.7 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 21.6 | 20.6 | 20.0 | 19.2 | 19.7 | 18.8 | 18.3 |
| 859 | 20.9 | 20.3 | 19.4 | 19.6 | 19.4 | 19.3 | 19.0 |
| 860 | 22.1 | 21.4 | 21.1 | 20.0 | 20.1 | 19.3 | 19.6 |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 21.4 | 21.0 | 20.4 | 18.9 | 19.9 | 19.3 | 19.2 |
| SD | 0.41 | 0.65 | 0.74 | 2.54 | 0.42 | 0.50 | 0.59 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 098
ABBR: TMCH

SEX: MALE
UNITS: pg

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 20.7 | 20.0 | 18.9 | 18.8 | 18.8 | 18.0 | 18.9 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 21.1 | 21.2 | 20.3 | -- | 19.6 | 18.5 | 19.4 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 21.7 | 21.1 | 19.6 | 19.7 | 19.0 | 18.2 | 18.3 |
| 890 | 21.3 | 20.9 | 19.4 | 19.8 | 18.7 | 17.8 | 18.2 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 21.6 | 21.5 | 19.7 | 19.4 | 21.2 | 18.4 | 18.4 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 21.9 | 20.5 | 19.2 | 18.3 | 18.2 | 17.7 | 18.2 |
| 896 | 20.6 | 20.8 | 19.5 | 18.9 | 19.0 | 19.1 | 18.7 |
| 897 | 21.5 | 20.6 | 19.3 | 18.5 | 18.7 | 17.9 | 18.4 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 20.5 | 21.0 | 20.1 | 19.7 | 19.5 | 18.1 | 18.9 |
| 900 | 22.3 | 22.2 | 19.9 | 19.1 | 19.0 | 17.8 | 19.1 |
| MEAN | 21.3 | 21.0 | 19.6 | 19.1 | 19.2 | 18.2 | 18.7 |
| SD | 0.59 | 0.60 | 0.43 | 0.55 | 0.82 | 0.42 | 0.41 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 18.9 | 18.9 | 18.1 | 18.1 |
| 923 | 22.2 | 20.7 | 18.3 | 17.7 | 18.6 | 18.4 | 19.0 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 20.3 | 19.6 | 17.9 | 17.6 | 18.6 | 17.7 | 18.4 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 19.7 | 18.5 | 16.9 | 17.3 | 18.1 | 17.9 | 18.3 |
| 930 | 21.8 | 21.0 | 20.0 | 18.5 | 19.6 | 18.7 | 19.3 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 20.1 | 20.4 | 19.2 | 20.5 | 19.1 | 18.8 |
| 933 | 19.8 | 19.3 | 17.5 | 16.4 | 16.7 | 16.4 | 17.1 |
| 934 | 22.2 | 21.5 | 19.3 | -- | -- | -- | -- |
| 935 | 21.9 | 20.8 | 18.8 | 19.5 | 19.8 | 19.4 | 20.2 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 19.9 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 21.1 | 20.4 | 18.7 | 18.3 | 19.8 | 18.9 | 18.9 |
| 940 | 20.1 | 19.0 | 18.6 | 17.2 | 18.1 | 17.7 | 18.3 |
| MEAN | 20.9 | 20.1 | 18.6 | 18.1 | 18.9 | 18.2 | 18.6 |
| SD | 1.05 | 0.96 | 1.08 | 0.99 | 1.10 | 0.87 | 0.82 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemo. Conc.

STUDY ID: 098
ABBR: TMCHC

SEX: MALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 801 | 35.4 | 34.9 | 36.1 | 36.2 | 36.8 | 35.9 | 36.1 |
| 802 | 35.0 | 35.5 | 36.8 | 36.6 | 36.5 | 35.9 | 35.5 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 35.4 | 35.7 | 36.3 | 37.2 | 36.1 | 36.9 | 35.5 |
| 807 | 35.4 | 35.6 | 36.6 | 37.2 | 37.2 | 35.8 | 36.5 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 35.2 | 35.4 | 38.1 | 36.3 | 37.0 | 36.4 | 36.5 |
| 810 | 35.0 | 35.5 | 36.0 | 36.4 | 36.2 | 35.5 | 40.7 |
| 811 | 35.4 | 35.4 | 36.3 | 37.4 | 35.6 | 35.8 | 37.1 |
| 812 | -- | -- | -- | 40.3 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 33.5 | 33.7 | 35.4 | 35.0 | 36.8 | 34.3 | 34.8 |
| 815 | 35.3 | 36.1 | 35.8 | 37.0 | 36.9 | 36.3 | 36.0 |
| 816 | 34.5 | 36.3 | 35.9 | 36.8 | 36.3 | 35.7 | 37.1 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 35.0 | 35.4 | 36.3 | 36.9 | 36.5 | 35.9 | 36.6 |
| SD | 0.60 | 0.71 | 0.74 | 1.30 | 0.49 | 0.68 | 1.62 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg. base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 34.8 | 34.7 | 36.0 | 36.7 | 35.9 | 36.0 | 36.0 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 34.8 | 35.0 | 37.2 | 36.0 | 37.0 | 34.4 | 36.5 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 33.7 | 34.8 | 36.0 | 35.5 | 35.3 | 35.0 | 34.8 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 35.9 | 35.0 | 36.2 | 36.1 | 36.2 | 35.7 | 36.4 |
| 851 | 34.9 | 35.7 | 35.9 | 21.4 | 36.3 | 36.3 | 37.1 |
| 852 | 34.3 | 35.1 | 36.8 | 36.4 | 36.2 | 36.6 | 36.6 |
| 853 | 33.9 | 34.6 | 35.7 | 35.7 | 35.7 | 35.5 | 35.5 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 35.9 | 35.0 | 36.2 | 36.1 | 37.0 | 35.8 | 35.7 |
| 859 | 35.5 | 35.5 | 36.0 | 36.9 | 36.0 | 36.0 | 36.2 |
| 860 | 35.1 | 35.3 | 37.1 | 36.9 | 36.7 | 35.9 | 37.1 |
| MEAN | 34.9 | 35.1 | 36.3 | 34.8 | 36.2 | 35.7 | 36.2 |
| SD | 0.76 | 0.35 | 0.53 | 4.72 | 0.55 | 0.63 | 0.72 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemo. Conc.

STUDY ID: 098
ABBR: TMCHC

SEX: MALE
UNITS: %

ANIMAL ID Week 2 Week 4 Week 8 Week 13 Week 16 Week 21 Week 27

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 35.3 | 35.8 | 35.4 | 36.5 | 35.6 | 35.7 | 36.4 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 34.9 | 35.1 | 36.7 | -- | 35.8 | 35.6 | 36.7 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 35.8 | 35.9 | 35.7 | 36.5 | 35.4 | 35.7 | 35.3 |
| 890 | 34.7 | 35.3 | 35.3 | 37.4 | 35.7 | 35.7 | 36.3 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 34.8 | 34.9 | 34.8 | 35.9 | 38.8 | 36.1 | 36.4 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 34.4 | 34.4 | 35.1 | 35.3 | 35.0 | 35.3 | 35.9 |
| 896 | 34.0 | 34.9 | 35.2 | 35.8 | 35.1 | 36.1 | 34.9 |
| 897 | 35.1 | 34.7 | 35.4 | 35.9 | 35.8 | 35.9 | 36.3 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 34.3 | 34.5 | 33.7 | 36.7 | 35.0 | 35.4 | 35.9 |
| 900 | 35.2 | 36.0 | 35.7 | 35.4 | 35.4 | 34.6 | 36.8 |
| MEAN | 34.9 | 35.2 | 35.3 | 36.2 | 35.8 | 35.6 | 36.1 |
| SD | 0.53 | 0.58 | 0.76 | 0.67 | 1.11 | 0.44 | 0.60 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 35.9 | 35.9 | 36.2 | 35.9 |
| 923 | 35.5 | 34.4 | 34.5 | 35.3 | 34.9 | 35.0 | 35.7 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 34.6 | 34.6 | 34.8 | 35.1 | 35.8 | 35.8 | 36.2 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 34.1 | 34.3 | 33.7 | 35.1 | 35.1 | 35.4 | 35.7 |
| 930 | 34.5 | 33.7 | 35.2 | 34.9 | 34.7 | 35.7 | 35.8 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 33.4 | 35.1 | 33.8 | 35.2 | 36.2 | 35.8 |
| 933 | 34.7 | 34.9 | 36.4 | 35.6 | 35.9 | 35.8 | 36.4 |
| 934 | 36.2 | 35.7 | 35.5 | -- | -- | -- | -- |
| 935 | 34.6 | 34.5 | 34.1 | 36.2 | 34.6 | 36.2 | 36.1 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 34.0 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 34.7 | 34.7 | 35.1 | 34.1 | 36.4 | 36.6 | 36.3 |
| 940 | 35.6 | 33.4 | 35.0 | 34.6 | 34.7 | 36.1 | 36.0 |
| MEAN | 34.9 | 34.4 | 34.9 | 35.1 | 35.3 | 35.9 | 36.0 |
| SD | 0.70 | 0.71 | 0.75 | 0.75 | 0.63 | 0.46 | 0.25 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes Count

STUDY ID: 098
ABBR: RETICS

SEX: MALE
UNITS: % RBCs

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 801 | 1.8 | 0.4 | 1.4 | 0.6 | 0.5 | 0.4 | 0.8 |
| 802 | 0.8 | 0.0 | 0.8 | 0.5 | 1.2 | 0.8 | 0.6 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 1.5 | 1.4 | 0.1 | 0.9 | 1.1 | 0.6 | 0.7 |
| 807 | 0.4 | 0.2 | 0.5 | 0.8 | 0.2 | 0.1 | 0.4 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 1.1 | 0.3 | 0.7 | 0.7 | 0.9 | 0.0 | 0.9 |
| 810 | 1.8 | 0.2 | 1.0 | 0.6 | 1.6 | 0.3 | 0.9 |
| 811 | 1.5 | 0.8 | 0.8 | 0.1 | 0.7 | 0.6 | 0.8 |
| 812 | -- | -- | -- | 0.7 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 0.1 | 0.2 | 0.7 | 0.9 | 0.7 | 0.3 | 1.0 |
| 815 | 1.3 | 0.7 | 1.3 | 0.7 | 1.0 | 0.6 | 0.8 |
| 816 | 1.7 | 0.4 | 0.2 | 0.5 | 1.5 | 0.8 | 0.6 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 1.2 | 0.5 | 0.8 | 0.6 | 0.9 | 0.5 | 0.8 |
| SD | 0.59 | 0.41 | 0.42 | 0.22 | 0.44 | 0.28 | 0.18 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 3.0 | 0.6 | 0.7 | 0.8 | 1.0 | 0.5 | 0.4 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 1.7 | 0.5 | 0.7 | 0.4 | 0.0 | 0.1 | 0.7 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 2.0 | 1.0 | 0.4 | 1.1 | 1.3 | 0.8 | 0.6 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 1.8 | 1.2 | 0.8 | 0.3 | 0.5 | 1.0 | 0.2 |
| 851 | 0.9 | 1.3 | 2.7 | 0.1 | 0.1 | 0.0 | 0.5 |
| 852 | 1.5 | 0.5 | 0.7 | 1.0 | 0.6 | 0.3 | 0.5 |
| 853 | 1.9 | 0.9 | 0.5 | 1.0 | 0.5 | 0.3 | 1.2 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 1.9 | 1.3 | QNS | 1.5 | 0.6 | 0.9 | 0.6 |
| 859 | 2.4 | 1.5 | 0.7 | 0.4 | 0.9 | 0.1 | 0.7 |
| 860 | 1.1 | 1.1 | 0.9 | 1.3 | 1.0 | 0.4 | 0.4 |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 1.8 | 1.0 | 0.9 | 0.8 | 0.7 | 0.4 | 0.6 |
| SD | 0.60 | 0.36 | 0.69 | 0.47 | 0.41 | 0.35 | 0.27 |
| N | 10 | 10 | 9 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

QNS-Quantity Not Sufficient

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes Count

STUDY ID: 098
ABBR: RETICS

SEX: MALE
UNITS: % RBCs

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 0.5 | 0.5 | 1.0 | 2.6 | 0.8 | 0.2 | 0.2 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 0.3 | 0.3 | 0.9 | -- | 0.9 | 0.2 | 0.6 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 0.2 | 1.9 | 1.8 | 1.1 | 1.9 | 0.3 | 1.0 |
| 890 | 1.0 | 0.6 | 1.5 | 1.0 | 1.1 | 0.7 | 1.5 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 1.8 | 0.7 | 1.2 | 1.0 | 0.5 | 0.2 | 1.0 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 2.3 | 1.2 | 2.1 | 3.4 | 1.6 | 0.0 | 1.0 |
| 896 | 2.2 | 0.9 | 0.4 | 0.8 | 0.9 | 0.1 | 0.2 |
| 897 | 1.2 | 0.6 | 2.6 | 1.1 | 0.6 | 0.9 | 0.7 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 2.3 | 0.7 | 2.5 | 0.8 | 2.0 | 0.4 | 0.6 |
| 900 | 2.7 | 0.5 | 1.9 | 2.1 | 0.7 | 0.0 | 0.5 |
| MEAN | 1.5 | 0.8 | 1.6 | 1.5 | 1.1 | 0.3 | 0.7 |
| SD | 0.93 | 0.46 | 0.72 | 0.93 | 0.54 | 0.29 | 0.40 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 1.9 | 0.3 | 0.2 | 1.3 |
| 923 | 3.6 | 1.5 | 3.3 | 2.3 | 1.2 | 0.3 | 0.4 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 5.3 | 2.6 | 1.2 | 0.6 | 0.4 | 0.0 | 0.8 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 5.7 | 0.5 | 2.4 | 1.1 | 1.4 | 0.4 | 0.6 |
| 930 | 5.3 | 1.0 | 1.6 | 1.2 | 0.9 | 0.3 | 0.6 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 4.4 | 2.8 | 2.1 | 1.0 | 0.3 | 0.6 |
| 933 | 4.7 | 1.9 | 2.6 | 1.6 | 1.2 | 0.4 | 0.5 |
| 934 | 1.8 | 3.2 | 4.1 | -- | -- | -- | -- |
| 935 | 2.8 | 0.3 | 3.4 | 1.7 | 0.8 | 0.6 | 0.0 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 3.0 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 4.5 | 2.2 | 1.5 | 2.9 | 1.0 | 0.0 | 0.6 |
| 940 | 3.5 | 1.1 | 1.3 | 2.2 | 1.4 | 0.2 | 1.0 |
| MEAN | 4.0 | 1.9 | 2.4 | 1.8 | 1.0 | 0.3 | 0.6 |
| SD | 1.28 | 1.28 | 1.00 | 0.67 | 0.38 | 0.18 | 0.35 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: 098
ABBR: NRBC

SEX: MALE
UNITS: COUNT

ANIMAL ID Week 2 Week 4 Week 8 Week 13 Week 16 Week 21 Week 27

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|-----|----|----|----|----|----|----|----|
| 801 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 802 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 807 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 810 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 811 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 812 | -- | -- | -- | 0 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 815 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 816 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|
| MEAN | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SD | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|-----|----|----|----|----|----|----|----|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 851 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 852 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 853 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 859 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 860 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

| | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|
| MEAN | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SD | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: 098
ABBR: NRBC

SEX: MALE
UNITS: COUNT

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 0 | 0 | 0 | -- | 0 | 0 | 0 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 890 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 896 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 897 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 900 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MEAN | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SD | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 0 | 0 | 0 | 0 |
| 923 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 930 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 0 | 1 | 1 | 0 | 0 | 0 |
| 933 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 934 | 0 | 0 | 0 | -- | -- | -- | -- |
| 935 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 1 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 940 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MEAN | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SD | 0.3 | 0.0 | 0.4 | 0.3 | 0.0 | 0.0 | 0.0 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: 098
ABBR: HB

SEX: MALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 801 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| 802 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 |
| 807 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 810 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 811 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 812 | -- | -- | -- | 0.0 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 815 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 816 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.31 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 0.0 | 0.1 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 |
| 851 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 |
| 852 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 853 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 859 | 0.0 | 0.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 860 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.03 | 0.22 | 0.12 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: 098
ABBR: HB

SEX: MALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 0.0 | 0.3 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 0.0 | 1.8 | 0.0 | 0.5 | 0.0 | 0.0 | 0.0 |
| 890 | 0.1 | 0.5 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 0.1 | 1.4 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 |
| 896 | 0.0 | 1.6 | 0.1 | 0.2 | 0.0 | 0.0 | 0.0 |
| 897 | 0.0 | 0.1 | 0.1 | 0.4 | 0.0 | 0.0 | 0.0 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 900 | 0.0 | 0.0 | 0.0 | 1.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.6 | 0.1 | 0.3 | 0.0 | 0.0 | 0.0 |
| SD | 0.05 | 0.73 | 0.08 | 0.32 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 0.4 | 0.0 | 0.0 | 0.0 |
| 923 | 3.5 | 0.7 | 0.2 | 0.7 | 0.0 | 0.3 | 0.0 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 2.0 | 0.7 | 0.3 | 1.0 | 0.0 | 0.0 | 0.0 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 2.8 | 0.2 | 0.4 | 0.8 | 0.1 | 0.0 | 0.0 |
| 930 | 1.4 | 0.8 | 0.3 | 1.2 | 0.0 | 0.0 | 0.0 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 0.7 | 0.0 | 1.2 | 0.0 | 0.0 | 0.0 |
| 933 | 0.7 | 1.2 | 0.4 | 0.3 | 0.1 | 0.0 | 0.0 |
| 934 | 3.1 | 0.0 | 0.0 | -- | -- | -- | -- |
| 935 | 1.8 | 0.5 | 1.1 | 0.8 | 0.0 | 0.0 | 0.0 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 3.3 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 2.3 | 0.0 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 |
| 940 | 1.7 | 0.7 | 0.4 | 0.7 | 0.0 | 0.0 | 0.0 |
| MEAN | 2.3 | 0.6 | 0.3 | 0.8 | 0.0 | 0.0 | 0.0 |
| SD | 0.91 | 0.38 | 0.32 | 0.32 | 0.04 | 0.09 | 0.00 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable



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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: 098
ABBR: %METHGB

SEX: MALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 801 | 0.0 | 0.0 | 1.0 | -- | 0.0 | 0.7 | 0.4 |
| 802 | 0.6 | 0.3 | 0.4 | 1.3 | 0.7 | 0.0 | 0.1 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 0.0 | 0.4 | 0.2 | 0.4 | 0.2 | 0.7 | 0.2 |
| 807 | 0.4 | 0.7 | 1.1 | 0.6 | 0.3 | 0.5 | 0.9 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 0.9 | 0.5 | 0.1 | 0.5 | 0.0 | 0.0 | 0.5 |
| 810 | 0.2 | 0.1 | 0.0 | 0.8 | 0.1 | 1.1 | 0.7 |
| 811 | 0.2 | 0.5 | 0.4 | 0.4 | 0.5 | 0.6 | 0.4 |
| 812 | -- | -- | -- | 0.5 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 0.7 | 2.5 | 0.4 | 0.6 | 1.0 | 0.2 | 0.2 |
| 815 | 1.3 | 1.0 | 0.2 | 0.3 | 0.0 | 0.0 | 0.0 |
| 816 | 0.1 | 0.6 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.4 | 0.7 | 0.4 | 0.5 | 0.3 | 0.4 | 0.3 |
| SD | 0.43 | 0.71 | 0.36 | 0.34 | 0.35 | 0.39 | 0.30 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 1.4 | 0.7 | 1.1 | 0.1 | 0.0 | 0.9 | 0.5 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 0.2 | 0.8 | 0.7 | 0.2 | 0.7 | 0.5 | 0.9 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 0.3 | 0.0 | 0.0 | 1.1 | 0.0 | 0.4 | 0.5 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 0.7 | 0.5 | 0.7 | 0.5 | 0.0 | 0.3 | 0.8 |
| 851 | 0.4 | 0.7 | 0.2 | 0.2 | 0.2 | 0.1 | 0.3 |
| 852 | 0.3 | 0.6 | 0.4 | 0.3 | 0.0 | 0.0 | 0.3 |
| 853 | 0.4 | 0.5 | 0.4 | 0.5 | 0.6 | 0.6 | 1.0 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 0.4 | 0.1 | 0.4 | 0.5 | 0.9 | 0.8 | 1.1 |
| 859 | 0.0 | 0.1 | 0.3 | 0.4 | 0.4 | 0.5 | 0.5 |
| 860 | 0.5 | 0.3 | 0.6 | 1.1 | 0.4 | 1.0 | 0.6 |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.5 | 0.4 | 0.5 | 0.5 | 0.3 | 0.5 | 0.7 |
| SD | 0.38 | 0.29 | 0.31 | 0.35 | 0.33 | 0.33 | 0.28 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: 098
ABBR: %METHGB

SEX: MALE
UNITS: %

ANIMAL ID Week 2 Week 4 Week 8 Week 13 Week 16 Week 21 Week 27

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 4.6 | 4.5 | 7.6 | 7.0 | 0.2 | 2.6 | 0.5 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 1.9 | 4.5 | 7.6 | -- | 0.4 | 0.5 | 1.3 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 2.3 | 5.4 | 6.7 | 8.9 | 0.0 | 0.2 | 0.5 |
| 890 | 0.5 | 3.0 | 4.9 | 6.4 | 0.5 | 0.2 | 0.5 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 3.2 | 5.3 | 6.3 | 5.6 | 0.8 | 0.4 | 1.0 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 1.4 | 4.6 | 7.1 | 7.4 | 0.9 | 0.8 | 1.8 |
| 896 | 2.2 | 4.5 | 7.1 | 7.8 | 0.0 | 0.1 | 0.9 |
| 897 | 1.3 | 3.8 | 7.4 | 7.4 | 0.0 | 0.4 | 0.6 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 1.7 | 3.3 | 6.0 | 5.7 | 0.0 | 0.2 | 0.0 |
| 900 | 1.3 | 4.7 | 5.9 | 6.4 | 0.7 | 0.4 | 1.6 |
| MEAN | 2.0 | 4.4 | 6.7 | 7.0 | 0.4 | 0.6 | 0.9 |
| SD | 1.15 | 0.78 | 0.88 | 1.06 | 0.36 | 0.74 | 0.56 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 11.4 | 1.8 | 0.5 | 0.4 |
| 923 | 14.3 | 14.7 | 11.1 | 12.0 | 2.4 | 1.6 | 0.6 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 12.6 | 10.9 | 9.8 | 13.3 | 2.9 | 1.0 | 1.4 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 17.3 | 8.9 | 12.0 | 12.5 | 1.2 | 0.4 | 0.8 |
| 930 | 8.6 | 6.1 | 7.1 | 9.3 | 0.7 | 0.0 | 1.3 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 12.2 | 7.7 | 12.6 | 0.6 | 0.5 | 0.8 |
| 933 | 10.5 | 7.8 | 9.0 | 13.3 | 1.8 | 0.0 | 0.4 |
| 934 | 11.6 | 7.3 | 9.6 | -- | -- | -- | -- |
| 935 | 9.3 | 8.8 | 9.6 | 11.7 | 1.0 | 0.1 | 0.4 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 40.5 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 15.2 | 10.9 | 10.6 | 12.6 | 0.1 | 0.6 | 0.6 |
| 940 | 15.1 | 9.2 | 8.9 | 11.6 | 0.8 | 0.0 | 0.7 |
| MEAN | 15.5 | 9.7 | 9.5 | 12.0 | 1.3 | 0.5 | 0.7 |
| SD | 9.22 | 2.54 | 1.48 | 1.17 | 0.88 | 0.51 | 0.36 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: 098
ABBR: PLT

SEX: MALE
UNITS: 10³/ccm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|-----|------|------|------|------|------|------|------|
| 801 | 1018 | 1070 | 1045 | 810 | 897 | 681 | 810 |
| 802 | 1301 | 1193 | 1178 | 983 | 1065 | 1035 | 1136 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 1280 | 1204 | 1248 | 1203 | 1074 | 1247 | 1164 |
| 807 | 1250 | 1225 | 1185 | 1193 | 1050 | 899 | 1076 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 1199 | 1142 | 1173 | 1091 | 1155 | 1233 | 1210 |
| 810 | 1245 | 1250 | 1098 | 1094 | 1076 | 884 | 794 |
| 811 | 1216 | 1186 | 1068 | 797 | 1046 | 1061 | 1149 |
| 812 | -- | -- | -- | 982 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 1309 | 906 | 1198 | 1161 | 461 | 1152 | 1268 |
| 815 | 1008 | 1206 | 1180 | 1114 | 1180 | 1137 | 1160 |
| 816 | 1264 | 1076 | 1030 | 1031 | 1046 | 1047 | 1141 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|-------|-------|------|-------|-------|-------|-------|
| MEAN | 1209 | 1146 | 1140 | 1042 | 1005 | 1038 | 1091 |
| SD | 108.8 | 103.3 | 74.0 | 139.4 | 205.3 | 175.0 | 160.2 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|-----|------|------|------|------|------|------|------|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 1563 | 1134 | 1251 | 1315 | 1240 | 1275 | 1290 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 1172 | 1127 | 1093 | 790 | 1014 | 926 | 1071 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 1250 | 1296 | 1293 | 1218 | 942 | 1112 | 1229 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 1254 | 1222 | 1178 | 1224 | 1124 | 1243 | 1193 |
| 851 | 1308 | 1303 | 963 | 937 | 623 | 711 | 944 |
| 852 | 1371 | 1326 | 1295 | 1312 | 1262 | 1316 | 1440 |
| 853 | 1325 | 1211 | 1229 | 1311 | 1126 | 1086 | 1123 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 1248 | 1238 | 1162 | 1077 | 906 | 1037 | 610 |
| 859 | 1033 | 1058 | 945 | 872 | 882 | 857 | 953 |
| 860 | 1159 | 813 | 1116 | 866 | 1128 | 1174 | 1113 |

| | | | | | | | |
|------|-------|-------|-------|-------|-------|-------|-------|
| MEAN | 1268 | 1173 | 1153 | 1092 | 1025 | 1074 | 1097 |
| SD | 141.3 | 152.7 | 124.8 | 209.3 | 193.3 | 194.7 | 227.2 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: 098
ABBR: PLT

SEX: MALE
UNITS: 10³/ccm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|-------|-------|------|-------|-------|-------|-------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 1295 | 1011 | 977 | 910 | 1044 | 983 | 659 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 1263 | 1318 | 1160 | -- | 724 | 1276 | 1179 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 1133 | 1141 | 1018 | 988 | 1059 | 1089 | 1078 |
| 890 | 1274 | 1250 | 1192 | 1147 | 869 | 1205 | 1177 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 1131 | 1162 | 1080 | 1214 | 572 | 1128 | 1136 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 1156 | 954 | 962 | 935 | 832 | 944 | 947 |
| 896 | 948 | 1203 | 1230 | 1121 | 1146 | 1053 | 1050 |
| 897 | 1084 | 1271 | 1138 | 1075 | 1170 | 1006 | 1107 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 1035 | 1146 | 1111 | 745 | 1095 | 1062 | 1107 |
| 900 | 877 | 1236 | 1199 | 987 | 1129 | 1164 | 1075 |
| MEAN | 1120 | 1169 | 1107 | 1014 | 964 | 1091 | 1052 |
| SD | 138.9 | 114.2 | 95.0 | 143.0 | 203.6 | 103.7 | 153.3 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|-------|-------|-------|-------|-------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 911 | 990 | 892 | 1011 |
| 923 | 1321 | 888 | 1179 | 656 | 909 | 872 | 941 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 1493 | 1396 | 1332 | 1204 | 1178 | 1068 | 1169 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 1072 | 990 | 1106 | 961 | 879 | 851 | 958 |
| 930 | 1162 | 1047 | 958 | 930 | 890 | 871 | 977 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 763 | 1041 | 1072 | 876 | 1002 | 1057 |
| 933 | 1329 | 1144 | 939 | 916 | 899 | 943 | 992 |
| 934 | 1032 | 1117 | 1063 | -- | -- | -- | -- |
| 935 | 1109 | 925 | 801 | 892 | 779 | 785 | 887 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 461 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 1123 | 1100 | 1063 | 959 | 1073 | 970 | 1036 |
| 940 | 1858 | 1321 | 1127 | 996 | 1142 | 1039 | 1029 |
| MEAN | 1196 | 1069 | 1061 | 950 | 962 | 929 | 1006 |
| SD | 358.4 | 192.4 | 144.2 | 139.3 | 129.9 | 90.3 | 76.3 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: 098
ABBR: APTT

SEX: MALE
UNITS: sec

ANIMAL ID Week 14 Week 27

GROUP: 0:0 mg base/kg/day

| | | |
|-----|------|------|
| 801 | -- | 14.8 |
| 802 | -- | 12.6 |
| 803 | 19.9 | -- |
| 804 | 17.1 | -- |
| 805 | 12.8 | -- |
| 806 | -- | 15.6 |
| 807 | -- | 15.4 |
| 808 | 15.7 | -- |
| 809 | -- | 15.4 |
| 810 | -- | 12.4 |
| 811 | -- | 16.6 |
| 812 | 18.3 | -- |
| 813 | 13.6 | -- |
| 814 | -- | 18.3 |
| 815 | -- | 13.8 |
| 816 | -- | 15.7 |
| 817 | 14.7 | -- |
| 818 | 15.9 | -- |
| 819 | 16.9 | -- |
| 820 | 16.8 | -- |

| | | |
|------|------|------|
| MEAN | 16.2 | 15.1 |
| SD | 2.13 | 1.78 |
| N | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | |
|-----|------|------|
| 841 | 16.9 | -- |
| 842 | 13.1 | -- |
| 843 | 15.2 | -- |
| 844 | -- | 15.7 |
| 845 | 16.8 | -- |
| 846 | -- | 15.3 |
| 847 | 13.4 | -- |
| 848 | -- | 15.0 |
| 849 | 12.0 | -- |
| 850 | -- | 13.7 |
| 851 | -- | 13.9 |
| 852 | -- | 12.7 |
| 853 | -- | 12.9 |
| 854 | 17.5 | -- |
| 855 | 12.8 | -- |
| 856 | 18.0 | -- |
| 857 | 17.2 | -- |
| 858 | -- | 18.3 |
| 859 | -- | 16.1 |
| 860 | -- | 11.5 |

| | | |
|------|------|------|
| MEAN | 15.3 | 14.5 |
| SD | 2.26 | 1.98 |
| N | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: 098
BBR: APTT

SEX: MALE
UNITS: sec

ANIMAL ID Week 14 Week 27

GROUP: 6.0:6.0 mg base/kg/day

| | | |
|-----|------|------|
| 881 | 14.8 | -- |
| 882 | 15.5 | -- |
| 883 | 13.7 | -- |
| 884 | -- | 16.4 |
| 885 | 9.4 | -- |
| 886 | 11.9 | -- |
| 887 | -- | 16.3 |
| 888 | 16.2 | -- |
| 889 | -- | 12.6 |
| 890 | -- | 15.5 |
| 891 | 13.6 | -- |
| 892 | 13.5 | -- |
| 893 | -- | 13.8 |
| 894 | 14.0 | -- |
| 895 | -- | 16.0 |
| 896 | -- | 12.7 |
| 897 | -- | 19.4 |
| 898 | 15.1 | -- |
| 899 | -- | 13.8 |
| 900 | -- | 17.5 |

| | | |
|------|------|------|
| MEAN | 13.8 | 15.4 |
| SD | 1.96 | 2.18 |
| N | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | |
|-----|------|------|
| 921 | -- | -- |
| 922 | -- | 13.1 |
| 923 | -- | 11.7 |
| 924 | 18.0 | -- |
| 925 | 18.9 | -- |
| 926 | -- | -- |
| 927 | -- | 18.1 |
| 928 | 13.5 | -- |
| 929 | -- | 16.5 |
| 930 | -- | 18.3 |
| 931 | 19.0 | -- |
| 932 | -- | 13.2 |
| 933 | -- | 13.2 |
| 934 | -- | -- |
| 935 | -- | 14.9 |
| 936 | -- | -- |
| 937 | -- | -- |
| 938 | 9.8 | -- |
| 939 | -- | 14.7 |
| 940 | -- | 14.7 |

| | | |
|------|------|------|
| MEAN | 15.8 | 14.8 |
| SD | 4.06 | 2.20 |
| N | 5 | 10 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: 098

SEX: MALE

ABBR: WBC

UNITS: $10^3/\text{cmm}$

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 801 | 14.0 | 13.5 | 12.9 | 12.7 | 11.4 | 13.7 | 9.0 |
| 802 | 13.6 | 14.9 | 15.6 | 11.8 | 11.4 | 8.6 | 12.0 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 18.9 | 20.6 | 15.2 | 14.8 | 13.0 | 13.2 | 13.0 |
| 807 | 17.4 | 16.3 | 18.2 | 14.7 | 14.5 | 13.2 | 13.0 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 26.1 | 20.8 | 20.9 | 16.4 | 16.5 | 16.2 | 17.1 |
| 810 | 19.4 | 22.3 | 20.1 | 16.5 | 17.9 | 19.6 | 16.5 |
| 811 | 12.9 | 14.4 | 12.8 | 12.0 | 12.3 | 12.4 | 11.3 |
| 812 | -- | -- | -- | 12.2 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 15.4 | 12.6 | 19.7 | 12.7 | 9.3 | 11.2 | 11.7 |
| 815 | 20.0 | 20.5 | 18.2 | 18.0 | 18.2 | 19.2 | 13.4 |
| 816 | 19.8 | 19.6 | 14.9 | 14.3 | 13.5 | 13.7 | 11.7 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 17.8 | 17.6 | 16.9 | 14.2 | 13.8 | 14.1 | 12.9 |
| SD | 3.99 | 3.57 | 2.96 | 2.10 | 2.96 | 3.40 | 2.41 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 23.0 | 11.2 | 10.6 | 15.3 | 8.6 | 14.2 | 10.3 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 24.0 | 22.7 | 19.9 | 17.5 | 14.7 | 15.5 | 14.9 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 16.3 | 12.1 | 14.8 | 14.6 | 9.8 | 12.5 | 11.6 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 20.9 | 19.0 | 20.1 | 17.3 | 15.4 | 15.6 | 16.6 |
| 851 | 15.7 | 17.1 | 13.9 | 10.4 | 11.9 | 12.3 | 14.9 |
| 852 | 16.0 | 14.5 | 17.9 | 14.1 | 11.4 | 13.4 | 15.5 |
| 853 | 13.2 | 10.3 | 12.4 | 11.1 | 10.9 | 10.6 | 10.0 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 20.2 | 20.0 | 20.8 | 16.1 | 12.6 | 13.9 | 13.0 |
| 859 | 14.5 | 13.5 | 13.0 | 11.0 | 12.3 | 10.7 | 9.9 |
| 860 | 27.1 | 17.8 | 22.7 | 19.2 | 18.4 | 19.9 | 24.6 |
| MEAN | 19.1 | 15.8 | 16.6 | 14.7 | 12.6 | 13.9 | 14.1 |
| SD | 4.63 | 4.13 | 4.17 | 3.03 | 2.88 | 2.74 | 4.42 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: 098
ABBR: WBC

SEX: MALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 21.7 | 27.3 | 24.7 | 21.8 | 12.8 | 13.7 | 10.5 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 21.2 | 21.8 | 21.4 | -- | 11.2 | 9.2 | 13.0 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 16.1 | 27.2 | 19.8 | 24.1 | 13.7 | 13.9 | 12.1 |
| 890 | 22.3 | 20.7 | 23.5 | 20.0 | 13.4 | 16.2 | 16.4 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 22.3 | 20.7 | 17.5 | 17.6 | 11.2 | 11.9 | 13.6 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 25.1 | 25.7 | 25.8 | 29.9 | 17.8 | 15.3 | 15.1 |
| 896 | 20.1 | 19.8 | 22.2 | 25.3 | 12.8 | 9.6 | 10.3 |
| 897 | 18.2 | 26.3 | 28.5 | 27.3 | 15.7 | 14.6 | 13.7 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 21.7 | 24.3 | 21.5 | 22.6 | 12.6 | 13.6 | 13.0 |
| 900 | 17.3 | 26.5 | 24.2 | 22.3 | 14.7 | 12.0 | 11.0 |
| MEAN | 20.6 | 24.0 | 22.9 | 23.4 | 13.6 | 13.0 | 12.9 |
| SD | 2.71 | 2.98 | 3.14 | 3.73 | 2.03 | 2.31 | 1.97 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 39.7 | 22.2 | 13.7 | 14.7 |
| 923 | 29.0 | 24.5 | 18.0 | 19.5 | 28.4 | 17.3 | 18.9 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 37.5 | 28.5 | 26.7 | 34.7 | 19.6 | 16.3 | 14.5 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 28.4 | 27.0 | 21.5 | 26.2 | 13.7 | 10.0 | 10.9 |
| 930 | 23.5 | 20.8 | 23.5 | 30.8 | 23.0 | 15.7 | 15.8 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 23.8 | 23.7 | 21.5 | 16.2 | 16.1 | 15.5 |
| 933 | 16.6 | 23.6 | 20.1 | 16.6 | 16.5 | 13.9 | 11.6 |
| 934 | 39.0 | 22.8 | 22.5 | -- | -- | -- | -- |
| 935 | 21.9 | 23.5 | 19.2 | 34.6 | 17.9 | 16.9 | 11.8 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 20.6 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 30.3 | 24.2 | 21.5 | 25.9 | 10.7 | 12.1 | 11.6 |
| 940 | 33.5 | 26.5 | 28.5 | 26.5 | 17.7 | 11.9 | 14.4 |
| MEAN | 28.0 | 24.5 | 22.5 | 27.6 | 18.6 | 14.4 | 14.0 |
| SD | 7.38 | 2.24 | 3.25 | 7.35 | 5.02 | 2.46 | 2.50 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: M. Neutrophils

STUDY ID: 098
ABBR: M. Neutrop

SEX: MALE
UNITS: 10³/cmm

ANIMAL ID Week 2 Week 4 Week 8 Week 13 Week 16 Week 21 Week 27

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 801 | 1.1 | 1.1 | 2.2 | 1.5 | 1.4 | 1.5 | 1.0 |
| 802 | 1.1 | 1.3 | 1.7 | 2.5 | 1.3 | 1.1 | 1.8 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 2.6 | 1.4 | 2.1 | 3.1 | 1.3 | 1.5 | 1.0 |
| 807 | 0.9 | 1.8 | 2.7 | 1.6 | 1.0 | 1.5 | 1.8 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 1.8 | 1.0 | 2.7 | 1.8 | 1.3 | 2.1 | 1.5 |
| 810 | 2.9 | 2.0 | 0.8 | 1.8 | 1.8 | 1.8 | 3.3 |
| 811 | 1.5 | 1.6 | 2.0 | 1.6 | 2.3 | 1.6 | 2.1 |
| 812 | -- | -- | -- | 1.0 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 1.1 | 0.3 | 6.9 | 3.0 | 1.0 | 0.6 | 0.9 |
| 815 | 1.4 | 2.1 | 1.3 | 0.4 | 0.4 | 1.0 | 1.3 |
| 816 | 1.6 | 1.2 | 1.5 | 1.9 | 1.4 | 1.1 | 1.9 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 1.6 | 1.4 | 2.4 | 1.8 | 1.3 | 1.4 | 1.7 |
| SD | 0.67 | 0.53 | 1.69 | 0.80 | 0.50 | 0.43 | 0.71 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|------|-----|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 3.0 | 2.0 | 0.5 | 1.7 | 1.7 | 2.4 | 1.5 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 0.7 | 1.8 | 1.6 | 2.3 | 0.4 | 1.6 | 2.7 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 1.1 | 1.7 | 1.2 | 1.3 | 1.0 | 1.3 | 1.3 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 2.7 | 1.5 | 2.6 | 2.1 | 1.5 | 14.0 | 1.0 |
| 851 | 2.0 | 2.2 | 1.3 | 2.1 | 0.8 | 1.8 | 1.8 |
| 852 | 0.8 | 1.7 | 3.0 | 2.7 | 0.8 | 1.7 | 3.7 |
| 853 | 2.8 | 0.4 | 1.6 | 1.8 | 1.9 | 1.3 | 1.7 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 2.0 | 2.4 | 2.3 | 2.4 | 1.0 | 1.0 | 2.0 |
| 859 | 1.9 | 1.2 | 0.8 | 1.2 | 1.6 | 0.6 | 0.6 |
| 860 | 1.6 | 1.1 | 1.8 | 2.7 | 1.5 | 2.0 | 6.4 |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 1.9 | 1.6 | 1.7 | 2.0 | 1.2 | 2.8 | 2.3 |
| SD | 0.82 | 0.58 | 0.78 | 0.53 | 0.48 | 3.98 | 1.69 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: M. Neutrophils

STUDY ID: 098
ABBR: M. Neutrop

SEX: MALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 3.9 | 2.7 | 3.0 | 2.6 | 1.4 | 1.5 | 0.4 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 4.2 | 4.4 | 2.8 | -- | 1.8 | 0.6 | 1.6 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 1.3 | 2.4 | 2.4 | 2.4 | 1.5 | 1.0 | 1.8 |
| 890 | 2.5 | 3.7 | 4.5 | 2.6 | 2.5 | 1.8 | 2.1 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 3.1 | 2.1 | 3.2 | 3.7 | 2.0 | 1.3 | 2.7 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 1.5 | 4.6 | 2.3 | 4.5 | 3.2 | 1.4 | 2.0 |
| 896 | 3.0 | 4.8 | 3.1 | 3.3 | 2.2 | 0.6 | 1.0 |
| 897 | 1.8 | 2.4 | 3.1 | 3.3 | 1.3 | 1.5 | 2.6 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 2.0 | 1.9 | 2.2 | 3.2 | 0.9 | 1.9 | 2.2 |
| 900 | 1.6 | 4.5 | 2.2 | 3.6 | 2.6 | 1.7 | 1.2 |
| MEAN | 2.5 | 3.4 | 2.9 | 3.2 | 1.9 | 1.3 | 1.8 |
| SD | 1.02 | 1.16 | 0.69 | 0.66 | 0.70 | 0.46 | 0.72 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 4.8 | 4.2 | 1.2 | 3.1 |
| 923 | 6.1 | 3.4 | 2.2 | 5.5 | 2.3 | 1.9 | 2.8 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 5.3 | 2.9 | 2.4 | 5.6 | 2.5 | 1.1 | 2.5 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 3.1 | 2.7 | 1.5 | 3.4 | 1.0 | 0.3 | 0.7 |
| 930 | 3.5 | 1.7 | 4.2 | 5.9 | 18.6 | 1.9 | 2.2 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 2.9 | 4.7 | 4.5 | 3.4 | 3.1 | 2.5 |
| 933 | 2.3 | 3.1 | 6.2 | 3.7 | 2.3 | 1.9 | 1.9 |
| 934 | 5.1 | 2.5 | 2.7 | -- | -- | -- | -- |
| 935 | 3.1 | 1.9 | 2.3 | 3.8 | 3.0 | 1.4 | 1.2 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 11.5 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 5.2 | 1.7 | 3.0 | 3.9 | 2.1 | 2.8 | 0.3 |
| 940 | 11.1 | 0.8 | 1.7 | 4.5 | 1.9 | 1.0 | 0.9 |
| MEAN | 5.6 | 2.4 | 3.1 | 4.6 | 4.1 | 1.7 | 1.8 |
| SD | 3.22 | 0.81 | 1.49 | 0.88 | 5.16 | 0.84 | 0.97 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: I. Neutrophils

STUDY ID: 098
ABBR: I. Neutrop

SEX: MALE
UNITS: $10^3/\text{cmm}$

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 801 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 802 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 807 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 810 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 811 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 812 | -- | -- | -- | 0.0 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 815 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 816 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 851 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 852 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 853 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 859 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 860 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.04 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: I. Neutrophils

STUDY ID: 098
ABBR: I. Neutrop

SEX: MALE
UNITS: 10³/cm³

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 890 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 896 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 897 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 900 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 0.0 | 0.0 | 0.0 | 0.0 |
| 923 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 930 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 933 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 934 | 0.0 | 0.0 | 0.0 | -- | -- | -- | -- |
| 935 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 0.0 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 940 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Lymphocytes

STUDY ID: 098
ABBR: Lymphocyte

SEX: MALE
UNITS: 10³/cm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 801 | 12.2 | 12.0 | 10.3 | 10.2 | 9.7 | 12.1 | 7.5 |
| 802 | 12.0 | 13.0 | 12.6 | 8.5 | 9.3 | 6.8 | 10.0 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 15.7 | 19.0 | 11.7 | 11.2 | 11.3 | 11.6 | 11.3 |
| 807 | 16.4 | 14.2 | 14.2 | 12.2 | 13.1 | 11.0 | 10.8 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 24.0 | 19.1 | 17.1 | 14.1 | 14.5 | 12.8 | 14.5 |
| 810 | 16.1 | 20.3 | 18.5 | 14.2 | 15.0 | 17.2 | 12.5 |
| 811 | 11.0 | 12.7 | 9.1 | 10.0 | 9.5 | 9.7 | 8.1 |
| 812 | -- | -- | -- | 10.5 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 14.0 | 12.0 | 11.4 | 8.6 | 7.9 | 9.6 | 10.2 |
| 815 | 18.4 | 17.4 | 16.4 | 16.2 | 16.9 | 18.0 | 11.5 |
| 816 | 17.8 | 18.4 | 13.1 | 12.2 | 11.9 | 11.5 | 9.2 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 15.8 | 15.8 | 13.4 | 11.6 | 11.9 | 12.0 | 10.6 |
| SD | 3.83 | 3.33 | 3.07 | 2.44 | 2.92 | 3.39 | 2.07 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 17.9 | 8.7 | 8.9 | 12.7 | 5.7 | 11.5 | 8.4 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 22.8 | 20.7 | 16.7 | 14.9 | 13.7 | 13.0 | 11.0 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 14.2 | 9.8 | 12.6 | 13.0 | 8.6 | 10.8 | 9.9 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 17.6 | 16.9 | 15.7 | 15.1 | 12.2 | 1.1 | 14.6 |
| 851 | 12.9 | 14.4 | 12.2 | 7.9 | 10.1 | 10.1 | 12.5 |
| 852 | 14.2 | 11.9 | 13.1 | 10.9 | 10.0 | 10.7 | 10.5 |
| 853 | 10.2 | 9.5 | 10.3 | 8.8 | 8.8 | 8.7 | 7.5 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 16.8 | 17.2 | 17.5 | 13.2 | 10.8 | 11.8 | 11.1 |
| 859 | 11.7 | 12.0 | 11.6 | 9.0 | 9.6 | 9.7 | 9.2 |
| 860 | 24.9 | 16.6 | 19.7 | 15.9 | 15.5 | 17.1 | 16.7 |
| MEAN | 16.3 | 13.8 | 13.8 | 12.1 | 10.5 | 10.5 | 11.1 |
| SD | 4.71 | 4.00 | 3.43 | 2.85 | 2.77 | 4.01 | 2.81 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

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WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Lymphocytes

STUDY ID: 098
ABBR: Lymphocyte

SEX: MALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 16.7 | 22.7 | 20.3 | 18.1 | 11.3 | 11.8 | 9.9 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 15.7 | 17.0 | 18.2 | -- | 8.4 | 8.2 | 9.9 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 14.3 | 22.6 | 16.4 | 21.2 | 11.8 | 12.8 | 9.8 |
| 890 | 19.6 | 15.7 | 18.1 | 17.0 | 10.1 | 14.3 | 13.9 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 19.0 | 17.0 | 14.0 | 12.7 | 8.2 | 9.9 | 9.4 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 22.6 | 18.8 | 20.6 | 22.7 | 14.2 | 12.9 | 11.8 |
| 896 | 16.7 | 14.7 | 17.3 | 20.7 | 10.1 | 8.9 | 9.1 |
| 897 | 15.1 | 20.8 | 23.7 | 22.1 | 13.7 | 11.8 | 10.7 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 19.3 | 21.9 | 17.8 | 18.8 | 11.1 | 11.0 | 10.0 |
| 900 | 14.9 | 18.8 | 18.9 | 15.8 | 11.0 | 9.8 | 8.7 |
| MEAN | 17.4 | 19.0 | 18.5 | 18.8 | 11.0 | 11.1 | 10.3 |
| SD | 2.65 | 2.90 | 2.62 | 3.27 | 1.96 | 1.94 | 1.52 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 31.0 | 16.9 | 12.2 | 11.3 |
| 923 | 21.5 | 18.4 | 14.8 | 12.3 | 23.9 | 14.7 | 14.7 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 31.5 | 23.7 | 21.6 | 25.3 | 16.3 | 14.5 | 11.6 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 23.0 | 16.5 | 17.6 | 21.5 | 11.1 | 8.9 | 9.9 |
| 930 | 20.0 | 15.8 | 16.2 | 22.5 | 2.1 | 13.3 | 12.6 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 18.8 | 15.9 | 14.8 | 11.8 | 12.6 | 12.4 |
| 933 | 12.1 | 18.9 | 12.5 | 10.6 | 13.4 | 11.7 | 8.8 |
| 934 | 33.2 | 18.0 | 18.0 | -- | -- | -- | -- |
| 935 | 16.9 | 21.4 | 15.4 | 28.0 | 14.3 | 14.5 | 10.1 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 8.0 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 21.8 | 15.7 | 15.5 | 18.6 | 7.5 | 8.7 | 10.9 |
| 940 | 22.4 | 19.3 | 23.9 | 17.2 | 15.4 | 10.7 | 13.0 |
| MEAN | 21.0 | 18.7 | 17.1 | 20.2 | 13.3 | 12.2 | 11.5 |
| SD | 7.69 | 2.48 | 3.36 | 6.71 | 5.83 | 2.21 | 1.72 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

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WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Monocytes

STUDY ID: 098
ABBR: Monocytes

SEX: MALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 801 | 0.7 | 0.3 | 0.3 | 1.0 | 0.2 | 0.1 | 0.5 |
| 802 | 0.5 | 0.4 | 1.2 | 0.7 | 0.7 | 0.7 | 0.1 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 0.6 | 0.2 | 1.4 | 0.4 | 0.4 | 0.0 | 0.4 |
| 807 | 0.0 | 0.3 | 1.1 | 0.4 | 0.4 | 0.5 | 0.3 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 0.3 | 0.2 | 0.6 | 0.2 | 0.7 | 1.0 | 0.5 |
| 810 | 0.2 | 0.0 | 0.8 | 0.3 | 1.1 | 0.2 | 0.5 |
| 811 | 0.4 | 0.1 | 1.5 | 0.2 | 0.4 | 0.9 | 1.0 |
| 812 | -- | -- | -- | 0.7 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 0.2 | 0.3 | 0.8 | 1.0 | 0.1 | 1.0 | 0.4 |
| 815 | 0.2 | 1.0 | 0.5 | 1.4 | 0.9 | 0.2 | 0.4 |
| 816 | 0.4 | 0.0 | 0.1 | 0.1 | 0.1 | 0.8 | 0.4 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 0.4 | 0.3 | 0.8 | 0.6 | 0.5 | 0.5 | 0.5 |
| SD | 0.21 | 0.29 | 0.47 | 0.41 | 0.34 | 0.39 | 0.23 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 1.8 | 0.3 | 1.1 | 0.8 | 0.9 | 0.1 | 0.2 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 0.5 | 0.2 | 1.6 | 0.2 | 0.6 | 0.6 | 1.0 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 0.2 | 0.6 | 0.7 | 0.1 | 0.1 | 0.4 | 0.3 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 0.2 | 0.2 | 1.4 | 0.2 | 1.4 | 0.5 | 0.8 |
| 851 | 0.8 | 0.3 | 0.4 | 0.4 | 0.8 | 0.1 | 0.3 |
| 852 | 1.0 | 0.1 | 1.6 | 0.4 | 0.5 | 0.5 | 1.2 |
| 853 | 0.3 | 0.3 | 0.4 | 0.6 | 0.2 | 0.6 | 0.8 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 0.8 | 0.4 | 0.8 | 0.3 | 0.5 | 0.6 | 0.0 |
| 859 | 0.7 | 0.3 | 0.5 | 0.4 | 1.1 | 0.2 | 0.0 |
| 860 | 0.3 | 0.2 | 1.1 | 0.6 | 1.5 | 0.6 | 1.0 |
| MEAN | 0.7 | 0.3 | 1.0 | 0.4 | 0.8 | 0.4 | 0.6 |
| SD | 0.49 | 0.14 | 0.47 | 0.22 | 0.47 | 0.21 | 0.45 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Monocytes

STUDY ID: 098
ABBR: Monocytes

SEX: MALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 0.7 | 1.6 | 1.2 | 1.1 | 0.0 | 0.3 | 0.1 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 1.3 | 0.2 | 0.4 | -- | 0.8 | 0.4 | 1.3 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 0.5 | 1.9 | 0.8 | 0.5 | 0.3 | 0.1 | 0.5 |
| 890 | 0.2 | 0.8 | 0.7 | 0.4 | 0.4 | 0.2 | 0.3 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 0.2 | 1.2 | 0.4 | 1.2 | 1.0 | 0.7 | 1.5 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 1.0 | 2.1 | 2.8 | 2.7 | 0.4 | 1.1 | 1.2 |
| 896 | 0.4 | 0.4 | 1.6 | 1.3 | 0.3 | 0.1 | 0.1 |
| 897 | 1.1 | 2.9 | 1.4 | 1.9 | 0.6 | 1.3 | 0.4 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 0.4 | 0.5 | 1.5 | 0.7 | 0.6 | 0.7 | 0.7 |
| 900 | 0.9 | 2.9 | 2.9 | 2.7 | 0.9 | 0.4 | 1.0 |
| MEAN | 0.7 | 1.5 | 1.4 | 1.4 | 0.5 | 0.5 | 0.7 |
| SD | 0.39 | 0.99 | 0.89 | 0.87 | 0.31 | 0.41 | 0.51 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 4.0 | 0.9 | 0.1 | 0.1 |
| 923 | 1.5 | 2.7 | 1.1 | 1.8 | 2.3 | 0.3 | 1.1 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 0.8 | 1.7 | 2.7 | 3.8 | 0.6 | 0.5 | 0.1 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 2.0 | 7.8 | 2.4 | 1.3 | 1.6 | 0.7 | 0.2 |
| 930 | 0.0 | 3.3 | 2.6 | 2.5 | 2.3 | 0.5 | 0.6 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 2.1 | 2.8 | 2.2 | 0.8 | 0.2 | 0.6 |
| 933 | 2.2 | 1.4 | 1.4 | 2.3 | 0.8 | 0.1 | 0.8 |
| 934 | 0.8 | 2.3 | 1.6 | -- | -- | -- | -- |
| 935 | 1.8 | 0.2 | 1.5 | 2.8 | 0.5 | 1.0 | 0.5 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 1.0 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 3.3 | 6.5 | 2.8 | 3.4 | 1.0 | 0.5 | 0.3 |
| 940 | 0.0 | 6.4 | 2.9 | 4.8 | 0.2 | 0.2 | 0.6 |
| MEAN | 1.3 | 3.4 | 2.2 | 2.9 | 1.1 | 0.4 | 0.5 |
| SD | 1.03 | 2.55 | 0.70 | 1.09 | 0.73 | 0.29 | 0.32 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Eosinophils

STUDY ID: 098
ABBR: Eosinophil

SEX: MALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 801 | 0.0 | 0.1 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 |
| 802 | 0.0 | 0.1 | 0.0 | 0.1 | 0.1 | 0.0 | 0.1 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.3 |
| 807 | 0.2 | 0.0 | 0.2 | 0.4 | 0.0 | 0.3 | 0.1 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 0.0 | 0.4 | 0.4 | 0.3 | 0.0 | 0.3 | 0.5 |
| 810 | 0.2 | 0.0 | 0.0 | 0.2 | 0.0 | 0.4 | 0.2 |
| 811 | 0.0 | 0.0 | 0.1 | 0.2 | 0.1 | 0.2 | 0.0 |
| 812 | -- | -- | -- | 0.0 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 0.2 | 0.1 | 0.6 | 0.0 | 0.3 | 0.0 | 0.2 |
| 815 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 816 | 0.0 | 0.0 | 0.1 | 0.1 | 0.1 | 0.3 | 0.2 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.1 | 0.1 | 0.2 | 0.1 | 0.1 | 0.2 | 0.2 |
| SD | 0.10 | 0.13 | 0.20 | 0.14 | 0.09 | 0.16 | 0.14 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 0.2 | 0.1 | 0.1 | 0.2 | 0.3 | 0.1 | 0.1 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.3 | 0.1 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 0.8 | 0.0 | 0.3 | 0.1 | 0.1 | 0.1 | 0.1 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 0.4 | 0.4 | 0.4 | 0.0 | 0.3 | 0.0 | 0.2 |
| 851 | 0.0 | 0.2 | 0.0 | 0.0 | 0.1 | 0.2 | 0.3 |
| 852 | 0.0 | 0.6 | 0.2 | 0.1 | 0.1 | 0.4 | 0.0 |
| 853 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 0.6 | 0.0 | 0.2 | 0.2 | 0.3 | 0.6 | 0.0 |
| 859 | 0.1 | 0.0 | 0.1 | 0.3 | 0.0 | 0.1 | 0.1 |
| 860 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.5 |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 | 0.2 | 0.1 |
| SD | 0.28 | 0.21 | 0.13 | 0.11 | 0.13 | 0.19 | 0.16 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Eosinophils

STUDY 10: 098
ABBR: Eosinophil

SEX: MALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 0.4 | 0.3 | 0.2 | 0.0 | 0.1 | 0.1 | 0.1 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 0.0 | 0.2 | 0.0 | -- | 0.2 | 0.0 | 0.3 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 0.0 | 0.3 | 0.2 | 0.0 | 0.1 | 0.0 | 0.0 |
| 890 | 0.0 | 0.4 | 0.2 | 0.0 | 0.4 | 0.0 | 0.0 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 |
| 896 | 0.0 | 0.0 | 0.2 | 0.0 | 0.3 | 0.0 | 0.1 |
| 897 | 0.2 | 0.3 | 0.3 | 0.0 | 0.2 | 0.0 | 0.0 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 |
| 900 | 0.0 | 0.3 | 0.2 | 0.2 | 0.1 | 0.1 | 0.1 |
| MEAN | 0.1 | 0.3 | 0.1 | 0.0 | 0.1 | 0.0 | 0.1 |
| SD | 0.13 | 0.14 | 0.12 | 0.07 | 0.13 | 0.04 | 0.10 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 0.0 | 0.2 | 0.1 | 0.1 |
| 923 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.3 | 0.2 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 0.0 | 0.3 | 0.0 | 0.0 | 0.2 | 0.2 | 0.3 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 |
| 930 | 0.0 | 0.0 | 0.5 | 0.0 | 0.0 | 0.0 | 0.3 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 0.0 | 0.2 | 0.0 | 0.2 | 0.3 | 0.0 |
| 933 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 |
| 934 | 0.0 | 0.0 | 0.2 | -- | -- | -- | -- |
| 935 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 0.0 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 0.0 | 0.2 | 0.2 | 0.0 | 0.1 | 0.1 | 0.0 |
| 940 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 |
| MEAN | 0.1 | 0.1 | 0.1 | 0.0 | 0.1 | 0.1 | 0.1 |
| SD | 0.11 | 0.12 | 0.17 | 0.00 | 0.10 | 0.11 | 0.12 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Basophils

STUDY ID: 098
ABBR: Basophils

SEX: MALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 801 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 802 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 803 | -- | -- | -- | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- | -- | -- | -- |
| 806 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 807 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 808 | -- | -- | -- | -- | -- | -- | -- |
| 809 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 810 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 811 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 812 | -- | -- | -- | 0.0 | -- | -- | -- |
| 813 | -- | -- | -- | -- | -- | -- | -- |
| 814 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 815 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 816 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 817 | -- | -- | -- | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 11 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 841 | -- | -- | -- | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- | -- | -- | -- |
| 844 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 845 | -- | -- | -- | -- | -- | -- | -- |
| 846 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 847 | -- | -- | -- | -- | -- | -- | -- |
| 848 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 849 | -- | -- | -- | -- | -- | -- | -- |
| 850 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 851 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 852 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 853 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 854 | -- | -- | -- | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- | -- | -- | -- |
| 858 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 859 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 860 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Basophils

STUDY ID: 098
ABBR: Basophils

SEX: MALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 881 | -- | -- | -- | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- | -- | -- | -- |
| 884 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 885 | -- | -- | -- | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- | -- | -- | -- |
| 887 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 888 | -- | -- | -- | -- | -- | -- | -- |
| 889 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 890 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 891 | -- | -- | -- | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- | -- | -- | -- |
| 893 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 894 | -- | -- | -- | -- | -- | -- | -- |
| 895 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 896 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 897 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 898 | -- | -- | -- | -- | -- | -- | -- |
| 899 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 900 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 921 | -- | -- | -- | -- | -- | -- | -- |
| 922 | -- | -- | -- | 0.0 | 0.0 | 0.0 | 0.0 |
| 923 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 924 | -- | -- | -- | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- | -- | -- | -- |
| 927 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 928 | -- | -- | -- | -- | -- | -- | -- |
| 929 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 930 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 931 | -- | -- | -- | -- | -- | -- | -- |
| 932 | -- | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 933 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 934 | 0.0 | 0.0 | 0.0 | -- | -- | -- | -- |
| 935 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 936 | -- | -- | -- | -- | -- | -- | -- |
| 937 | 0.0 | -- | -- | -- | -- | -- | -- |
| 938 | -- | -- | -- | -- | -- | -- | -- |
| 939 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 940 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: 098
ABBR: RBC

SEX: FEMALE
UNITS: 10⁶/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 7.55 | 7.25 | 8.06 | 8.20 | 8.04 | 8.68 | 8.50 |
| 824 | 6.72 | 6.83 | 7.66 | -- | 6.85 | 7.61 | 7.30 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 7.45 | 7.49 | 7.68 | 7.97 | 7.54 | 8.14 | 7.22 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 7.00 | 7.00 | 7.91 | 7.61 | 8.04 | 8.07 | 8.11 |
| 831 | 7.06 | 7.12 | 7.66 | 7.49 | 7.42 | 7.78 | 7.49 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 7.33 | 7.76 | 7.76 | 8.28 | 8.00 | 8.50 | 8.16 |
| 835 | 7.30 | 7.61 | 7.94 | 7.97 | 7.79 | 8.49 | 7.66 |
| 836 | 7.15 | 7.25 | 7.89 | 7.95 | 7.68 | 8.16 | 8.00 |
| 837 | 7.76 | 7.98 | 7.90 | 7.43 | 7.80 | 7.80 | 7.78 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 7.43 | 7.56 | 8.09 | 7.93 | 7.64 | 7.89 | 7.76 |
| MEAN | 7.28 | 7.39 | 7.86 | 7.87 | 7.68 | 8.11 | 7.80 |
| SD | 0.301 | 0.357 | 0.159 | 0.298 | 0.360 | 0.354 | 0.403 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|-------|-------|-------|-------|-------|-------|-------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 861 | 7.66 | 7.63 | 8.57 | 7.93 | 7.18 | 7.92 | 7.92 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 7.19 | 7.93 | 7.95 | 8.19 | 7.42 | 7.69 | 7.50 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 6.78 | 7.27 | 7.64 | 7.58 | 7.56 | 8.11 | 7.22 |
| 868 | 6.79 | 7.83 | 8.23 | 8.02 | -- | 8.50 | 8.05 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 6.95 | 6.77 | 7.64 | 6.97 | 6.80 | 7.36 | 7.73 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 6.82 | 6.91 | 7.64 | 7.33 | 7.07 | 7.89 | 6.87 |
| 874 | 6.42 | 7.56 | 7.56 | 7.09 | 7.47 | 7.85 | 7.23 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 7.29 | 7.16 | 7.76 | 7.72 | 7.69 | 8.14 | 7.86 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 7.28 | 7.39 | 7.83 | 8.12 | 7.95 | 8.42 | 8.28 |
| 880 | 7.19 | 6.91 | 6.79 | 7.84 | 7.68 | 7.84 | 7.51 |
| MEAN | 7.04 | 7.34 | 7.76 | 7.68 | 7.42 | 7.97 | 7.62 |
| SD | 0.353 | 0.402 | 0.465 | 0.427 | 0.355 | 0.337 | 0.432 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: 098
ABBR: RBC

SEX: FEMALE
UNITS: 10⁶/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 6.88 | 6.54 | 7.34 | 7.04 | 7.27 | 8.00 | 7.80 |
| 902 | 7.16 | 7.37 | 7.06 | 7.34 | 7.28 | 7.58 | 7.61 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 7.19 | 7.02 | 7.94 | 7.30 | -- | 8.49 | 7.73 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 6.94 | 6.93 | 7.11 | 8.16 | 7.33 | 8.00 | 7.94 |
| 909 | 7.07 | 7.36 | 7.65 | 7.19 | 8.02 | 8.58 | 8.16 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 7.09 | 7.39 | 6.93 | -- | 7.99 | 8.04 | 7.86 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 6.94 | 6.80 | 7.50 | 6.98 | 7.32 | 7.65 | 7.48 |
| 916 | 7.37 | 6.71 | 7.05 | 6.93 | 7.56 | 7.79 | 7.37 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 6.32 | 6.64 | 6.70 | 6.71 | 6.00 | 7.66 | 7.19 |
| 919 | 6.84 | 6.97 | 7.32 | 7.44 | 7.73 | 8.25 | 8.16 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 6.98 | 6.97 | 7.26 | 7.23 | 7.39 | 8.00 | 7.73 |
| SD | 0.282 | 0.313 | 0.367 | 0.416 | 0.599 | 0.349 | 0.322 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|-------|-------|-------|-------|-------|-------|-------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 5.65 | 6.65 | 7.94 | 6.56 | 7.07 | 8.27 | 7.51 |
| 942 | 6.01 | 6.43 | 7.01 | 6.83 | 6.94 | 8.59 | 7.70 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 6.19 | 6.83 | 7.56 | 6.92 | 7.75 | 8.33 | 8.54 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 6.59 | 6.55 | 7.35 | 7.63 | 7.94 | 8.16 | 7.94 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 6.01 | 7.35 | 7.25 | 5.25 | 7.39 | 8.26 | 7.44 |
| 954 | 6.18 | 7.00 | 7.55 | 7.25 | 7.61 | 8.46 | 7.98 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 6.69 | 6.87 | 8.14 | 5.92 | 7.79 | -- | -- |
| 957 | 5.79 | 7.13 | 8.04 | 7.56 | 7.99 | 8.56 | 7.83 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 6.07 | 6.36 | 7.12 | 6.98 | 7.32 | 7.84 | 7.13 |
| 960 | 6.70 | 7.43 | 7.48 | 7.57 | 7.71 | 8.15 | 7.86 |
| MEAN | 6.19 | 6.86 | 7.54 | 6.85 | 7.55 | 8.29 | 7.77 |
| SD | 0.365 | 0.370 | 0.388 | 0.769 | 0.358 | 0.233 | 0.398 |
| N | 10 | 10 | 10 | 10 | 10 | 9 | 9 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: 098
ABBR: THGB

SEX: FEMALE
UNITS: g/dL

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 15.7 | 15.3 | 16.5 | 16.6 | 16.8 | 17.3 | 16.6 |
| 824 | 15.3 | 15.1 | 16.3 | -- | 15.3 | 16.1 | 15.8 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 16.4 | 16.0 | 16.8 | 15.4 | 15.1 | 17.0 | 15.3 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 15.9 | 15.7 | 16.5 | 16.0 | 17.4 | 16.8 | 16.8 |
| 831 | 15.1 | 15.0 | 15.3 | 14.9 | 15.2 | 15.4 | 14.7 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 15.5 | 15.9 | 15.4 | 16.5 | 16.1 | 16.8 | 16.0 |
| 835 | 15.7 | 15.9 | 17.0 | 16.1 | 16.1 | 16.6 | 15.8 |
| 836 | 15.8 | 15.8 | 16.3 | 16.8 | 16.4 | 16.8 | 16.1 |
| 837 | 16.6 | 16.7 | 16.4 | 15.4 | 16.7 | 16.2 | 16.3 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 15.6 | 16.0 | 17.0 | 16.3 | 15.8 | 15.9 | 16.0 |
| MEAN | 15.8 | 15.7 | 16.4 | 16.0 | 16.1 | 16.5 | 15.9 |
| SD | 0.46 | 0.50 | 0.59 | 0.64 | 0.76 | 0.58 | 0.61 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 861 | 15.9 | 15.8 | 17.0 | 16.0 | 15.0 | 15.8 | 15.5 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 15.2 | 16.5 | 16.9 | 16.3 | 15.1 | 15.8 | 15.4 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 15.0 | 15.8 | 16.4 | 16.1 | 16.6 | 17.2 | 15.1 |
| 868 | 15.5 | 17.2 | 17.9 | 16.8 | -- | 16.8 | 17.0 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 15.5 | 15.0 | 16.5 | 14.9 | 15.9 | 15.3 | 16.0 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 15.8 | 16.0 | 17.0 | 16.5 | 16.3 | 17.4 | 16.3 |
| 874 | 13.8 | 15.8 | 15.7 | 14.7 | 15.5 | 15.7 | 14.7 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 16.1 | 15.7 | 16.3 | 15.8 | 16.6 | 16.8 | 15.6 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 15.0 | 15.2 | 15.8 | 15.9 | 16.1 | 16.3 | 16.1 |
| 880 | 15.7 | 15.1 | 15.0 | 15.7 | 15.8 | 15.8 | 15.2 |
| MEAN | 15.4 | 15.8 | 16.5 | 15.9 | 15.9 | 16.3 | 15.7 |
| SD | 0.66 | 0.67 | 0.82 | 0.65 | 0.59 | 0.72 | 0.67 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: 098
ABBR: THGB

SEX: FEMALE
UNITS: g/dL

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 14.8 | 14.7 | 15.7 | 15.4 | 16.0 | 16.6 | 15.7 |
| 902 | 15.2 | 15.6 | 14.9 | 14.8 | 15.5 | 15.2 | 15.2 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 15.6 | 15.1 | 16.4 | 15.5 | -- | 17.0 | 15.7 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 14.6 | 15.0 | 15.4 | 18.1 | 16.2 | 16.2 | 15.7 |
| 909 | 14.9 | 15.9 | 15.6 | 15.2 | 16.8 | 16.3 | 15.9 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 15.0 | 16.1 | 15.6 | -- | 16.4 | 15.7 | 15.3 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 15.1 | 15.6 | 16.2 | 15.5 | 16.3 | 16.2 | 15.6 |
| 916 | 16.1 | 15.4 | 15.9 | 15.3 | 17.0 | 16.1 | 15.4 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 14.4 | 14.3 | 14.4 | 14.5 | 12.6 | 16.0 | 14.6 |
| 919 | 15.0 | 15.2 | 15.8 | 15.6 | 16.8 | 16.2 | 16.1 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 15.1 | 15.3 | 15.6 | 15.5 | 16.0 | 16.2 | 15.5 |
| SD | 0.49 | 0.55 | 0.59 | 1.02 | 1.34 | 0.48 | 0.42 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 11.6 | 14.3 | 16.2 | 13.2 | 15.1 | 16.2 | 15.2 |
| 942 | 12.9 | 13.2 | 15.3 | 13.2 | 15.5 | 18.2 | 16.4 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 13.0 | 13.3 | 15.1 | 13.6 | 15.8 | 16.0 | 15.8 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 14.3 | 14.1 | 14.5 | 14.6 | 16.0 | 15.8 | 15.5 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 13.5 | 15.4 | 15.3 | 11.0 | 15.7 | 16.5 | 15.3 |
| 954 | 13.1 | 14.0 | 14.3 | 13.6 | 15.2 | 16.0 | 15.7 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 13.7 | 13.6 | 15.5 | 13.5 | 15.5 | -- | -- |
| 957 | 12.0 | 14.0 | 15.3 | 14.6 | 16.2 | 16.3 | 15.9 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 13.2 | 13.4 | 14.4 | 13.4 | 15.3 | 15.6 | 14.5 |
| 960 | 13.9 | 15.7 | 15.7 | 14.7 | 16.1 | 16.1 | 15.9 |
| MEAN | 13.1 | 14.1 | 15.2 | 13.5 | 15.6 | 16.3 | 15.6 |
| SD | 0.82 | 0.85 | 0.61 | 1.07 | 0.38 | 0.76 | 0.54 |
| N | 10 | 10 | 10 | 10 | 10 | 9 | 9 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: 098
ABBR: HCT

SEX: FEMALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 44.1 | 42.7 | 44.6 | 45.4 | 45.0 | 48.1 | 45.8 |
| 824 | 40.9 | 41.1 | 44.1 | -- | 39.9 | 43.2 | 41.9 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 44.5 | 44.6 | 44.4 | 43.8 | 44.0 | 45.7 | 40.0 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 42.5 | 43.5 | 45.3 | 43.1 | 45.9 | 46.4 | 46.2 |
| 831 | 41.8 | 41.4 | 42.0 | 40.1 | 40.4 | 42.6 | 40.2 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 41.9 | 42.8 | 41.2 | 43.5 | 43.0 | 46.0 | 42.8 |
| 835 | 42.1 | 43.7 | 43.9 | 43.1 | 43.7 | 46.8 | 43.4 |
| 836 | 43.6 | 43.3 | 44.3 | 44.4 | 44.4 | 45.9 | 44.5 |
| 837 | 44.9 | 46.4 | 44.2 | 41.8 | 44.3 | 43.9 | 43.3 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 41.8 | 43.1 | 44.7 | 43.0 | 42.6 | 42.8 | 42.5 |
| MEAN | 42.8 | 43.3 | 43.9 | 43.1 | 43.3 | 45.1 | 43.1 |
| SD | 1.36 | 1.51 | 1.27 | 1.51 | 1.92 | 1.88 | 2.08 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 861 | 44.1 | 43.3 | 46.8 | 42.9 | 40.1 | 43.2 | 42.8 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 42.3 | 45.6 | 45.0 | 45.8 | 43.0 | 44.0 | 42.2 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 42.1 | 44.2 | 44.5 | 43.6 | 44.9 | 47.2 | 41.5 |
| 868 | 41.5 | 47.4 | 48.6 | 46.1 | -- | 49.3 | 46.4 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 42.3 | 41.2 | 45.0 | 40.7 | 40.3 | 42.7 | 44.0 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 43.7 | 44.5 | 46.9 | 44.9 | 44.0 | 48.5 | 45.4 |
| 874 | 37.6 | 44.2 | 43.3 | 39.3 | 41.6 | 43.6 | 40.2 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 42.8 | 43.1 | 44.5 | 42.8 | 44.1 | 46.2 | 43.2 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 40.8 | 42.3 | 43.5 | 44.1 | 43.8 | 45.6 | 44.2 |
| 880 | 42.7 | 40.5 | 39.4 | 42.6 | 43.0 | 43.4 | 41.0 |
| MEAN | 42.0 | 43.6 | 44.8 | 43.3 | 42.8 | 45.4 | 43.1 |
| SD | 1.82 | 2.04 | 2.50 | 2.14 | 1.72 | 2.36 | 1.96 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Hematocrit

STUDY ID: 098
ABBR: HCT

SEX: FEMALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 40.4 | 39.3 | 43.3 | 40.4 | 42.7 | 44.2 | 42.4 |
| 902 | 42.6 | 43.7 | 41.9 | 41.3 | 41.6 | 42.4 | 42.2 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 41.9 | 41.3 | 44.9 | 42.0 | -- | 46.5 | 42.3 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 39.8 | 41.2 | 41.2 | 47.7 | 43.8 | 44.3 | 42.8 |
| 909 | 40.0 | 43.1 | 43.4 | 41.1 | 45.5 | 46.1 | 43.7 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 42.0 | 44.0 | 41.0 | -- | 44.0 | 44.3 | 42.0 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 41.3 | 41.7 | 43.6 | 41.2 | 43.3 | 43.1 | 42.1 |
| 916 | 44.5 | 41.9 | 42.5 | 42.4 | 45.5 | 45.6 | 42.7 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 38.6 | 40.8 | 40.2 | 39.4 | 36.2 | 43.8 | 40.2 |
| 919 | 40.2 | 41.7 | 42.3 | 43.1 | 46.2 | 46.0 | 45.1 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 41.1 | 41.9 | 42.4 | 42.1 | 43.2 | 44.6 | 42.6 |
| SD | 1.69 | 1.41 | 1.41 | 2.37 | 3.01 | 1.37 | 1.25 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 33.6 | 40.7 | 45.0 | 37.3 | 41.9 | 44.4 | 41.1 |
| 942 | 35.2 | 38.5 | 39.5 | 40.3 | 42.3 | 47.9 | 43.5 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 35.7 | 38.2 | 40.6 | 35.8 | 42.0 | 42.7 | 44.3 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 39.4 | 39.6 | 40.6 | 40.5 | 44.2 | 43.1 | 42.0 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 36.0 | 44.5 | 41.8 | 30.5 | 44.4 | 46.1 | 42.6 |
| 954 | 36.0 | 40.7 | 41.3 | 37.7 | 42.8 | 44.7 | 43.0 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 38.6 | 38.6 | 43.5 | 30.7 | 43.1 | -- | -- |
| 957 | 33.4 | 40.9 | 42.7 | 40.1 | 44.5 | 45.2 | 43.1 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 36.2 | 37.5 | 39.2 | 37.6 | 41.4 | 42.2 | 38.7 |
| 960 | 38.3 | 44.7 | 42.2 | 41.1 | 42.9 | 44.0 | 43.2 |
| MEAN | 36.2 | 40.4 | 41.6 | 37.2 | 43.0 | 44.5 | 42.4 |
| SD | 2.01 | 2.50 | 1.80 | 3.85 | 1.10 | 1.78 | 1.65 |
| N | 10 | 10 | 10 | 10 | 10 | 9 | 9 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: 098
ABBR: MCV

SEX: FEMALE
UNITS: fl.

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 58.4 | 58.9 | 55.3 | 55.4 | 56.0 | 55.4 | 53.9 |
| 824 | 60.9 | 60.2 | 57.6 | -- | 58.2 | 56.8 | 57.4 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 59.7 | 59.5 | 57.8 | 55.0 | 58.4 | 56.1 | 55.4 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 60.7 | 62.1 | 57.3 | 56.6 | 57.1 | 57.5 | 57.0 |
| 831 | 59.2 | 58.1 | 54.8 | 53.5 | 54.4 | 54.8 | 53.7 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 57.2 | 55.2 | 53.1 | 52.5 | 53.8 | 54.1 | 52.5 |
| 835 | 57.7 | 57.4 | 55.3 | 54.1 | 56.1 | 55.1 | 56.7 |
| 836 | 61.0 | 59.7 | 56.1 | 55.8 | 57.8 | 56.3 | 55.6 |
| 837 | 57.9 | 58.1 | 55.9 | 56.3 | 56.8 | 56.3 | 55.7 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 56.3 | 57.0 | 55.3 | 54.2 | 55.8 | 54.2 | 54.8 |
| MEAN | 58.9 | 58.6 | 55.9 | 54.8 | 56.4 | 55.7 | 55.3 |
| SD | 1.66 | 1.91 | 1.44 | 1.36 | 1.53 | 1.12 | 1.57 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 861 | 57.6 | 56.7 | 54.6 | 54.1 | 55.8 | 54.5 | 54.0 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 58.8 | 57.5 | 56.6 | 55.9 | 58.0 | 57.2 | 56.3 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 62.1 | 60.8 | 58.2 | 57.5 | 59.4 | 58.2 | 57.5 |
| 868 | 61.1 | 60.5 | 59.1 | 57.5 | -- | 58.0 | 57.6 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 60.9 | 60.9 | 58.9 | 58.4 | 59.3 | 58.0 | 56.9 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 64.1 | 64.4 | 61.4 | 61.3 | 62.2 | 61.5 | 66.1 |
| 874 | 58.6 | 58.5 | 57.3 | 55.4 | 55.7 | 55.5 | 55.6 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 58.7 | 60.2 | 57.3 | 55.4 | 57.3 | 56.8 | 55.0 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 56.0 | 57.2 | 55.6 | 54.3 | 55.1 | 54.2 | 53.4 |
| 880 | 59.4 | 58.6 | 58.0 | 54.3 | 56.0 | 55.4 | 54.6 |
| MEAN | 59.7 | 59.5 | 57.7 | 56.4 | 57.6 | 56.9 | 56.7 |
| SD | 2.35 | 2.31 | 1.91 | 2.28 | 2.32 | 2.18 | 3.60 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: 098
ABBR: MCV

SEX: FEMALE
UNITS: fl.

ANIMAL ID Week 2 Week 4 Week 8 Week 13 Week 16 Week 21 Week 27

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 901 | 58.7 | 60.1 | 59.0 | 57.4 | 58.7 | 55.3 | 54.4 |
| 902 | 59.5 | 59.3 | 59.3 | 56.3 | 57.1 | 55.9 | 55.5 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 58.3 | 58.8 | 56.5 | 57.5 | -- | 54.8 | 54.7 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 57.3 | 59.5 | 57.9 | 58.5 | 59.8 | 55.4 | 53.9 |
| 909 | 56.6 | 58.6 | 56.7 | 57.2 | 56.7 | 53.7 | 53.6 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 59.2 | 59.5 | 59.2 | -- | 55.1 | 55.1 | 53.4 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 59.5 | 61.3 | 58.1 | 59.0 | 59.2 | 56.3 | 56.3 |
| 916 | 60.4 | 62.4 | 60.3 | 61.2 | 60.2 | 58.5 | 57.9 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 61.1 | 61.4 | 60.0 | 58.7 | 60.3 | 57.2 | 55.9 |
| 919 | 58.8 | 59.8 | 57.8 | 57.9 | 59.8 | 55.8 | 55.3 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 58.9 | 60.1 | 58.5 | 58.2 | 58.5 | 55.8 | 55.1 |
| SD | 1.34 | 1.24 | 1.30 | 1.41 | 1.83 | 1.33 | 1.39 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 941 | 59.5 | 61.2 | 56.7 | 56.9 | 59.3 | 53.7 | 54.7 |
| 942 | 58.6 | 59.9 | 56.3 | 59.0 | 61.0 | 55.8 | 56.5 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 57.7 | 55.9 | 53.7 | 51.7 | 54.2 | 51.3 | 51.9 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 59.8 | 60.5 | 55.2 | 53.1 | 55.7 | 52.8 | 52.9 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 59.9 | 60.5 | 57.7 | 58.1 | 60.1 | 55.8 | 57.3 |
| 954 | 58.3 | 58.1 | 54.4 | 52.0 | 56.2 | 52.8 | 53.9 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 57.7 | 56.2 | 53.4 | 51.9 | 55.3 | -- | -- |
| 957 | 57.7 | 57.4 | 53.1 | 53.0 | 55.7 | 52.8 | 55.0 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 59.6 | 59.0 | 55.1 | 53.9 | 56.6 | 53.8 | 54.3 |
| 960 | 57.2 | 60.2 | 56.4 | 54.3 | 55.6 | 54.0 | 55.0 |
| MEAN | 58.6 | 58.9 | 55.2 | 54.4 | 57.0 | 53.6 | 54.6 |
| SD | 1.02 | 1.89 | 1.55 | 2.67 | 2.30 | 1.46 | 1.66 |
| N | 10 | 10 | 10 | 10 | 10 | 9 | 9 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 098
ABBR: TMCH

SEX: FEMALE
UNITS: pg

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 20.8 | 21.1 | 20.5 | 20.2 | 20.9 | 19.9 | 19.5 |
| 824 | 22.8 | 22.1 | 21.3 | -- | 22.3 | 21.2 | 21.6 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 22.0 | 21.4 | 21.9 | 19.3 | 20.0 | 20.9 | 21.2 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 22.7 | 22.4 | 20.9 | 21.0 | 21.6 | 20.8 | 20.7 |
| 831 | 21.4 | 21.1 | 20.0 | 19.9 | 20.5 | 19.8 | 19.6 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 21.1 | 20.5 | 19.8 | 19.9 | 20.1 | 19.8 | 19.6 |
| 835 | 21.5 | 20.9 | 21.4 | 20.2 | 20.7 | 19.6 | 20.6 |
| 836 | 22.1 | 21.8 | 20.7 | 21.1 | 21.4 | 20.6 | 20.1 |
| 837 | 21.4 | 20.9 | 20.8 | 20.7 | 21.4 | 20.8 | 21.0 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 21.0 | 21.2 | 21.0 | 20.6 | 20.7 | 20.2 | 20.6 |
| MEAN | 21.7 | 21.3 | 20.8 | 20.3 | 21.0 | 20.4 | 20.5 |
| SD | 0.69 | 0.59 | 0.63 | 0.58 | 0.72 | 0.57 | 0.73 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 861 | 20.8 | 20.7 | 19.8 | 20.2 | 20.9 | 19.9 | 19.6 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 21.1 | 20.8 | 21.3 | 19.9 | 20.4 | 20.5 | 20.5 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 22.1 | 21.7 | 21.5 | 21.2 | 22.0 | 21.2 | 20.9 |
| 868 | 22.8 | 22.0 | 21.7 | 20.9 | -- | 19.8 | 21.1 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 22.3 | 22.2 | 21.6 | 21.4 | 23.4 | 20.8 | 20.7 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 23.2 | 23.2 | 22.3 | 22.5 | 23.1 | 22.1 | 23.7 |
| 874 | 21.5 | 20.9 | 20.8 | 20.7 | 20.7 | 20.0 | 20.3 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 22.1 | 21.9 | 21.0 | 20.5 | 21.6 | 20.6 | 19.8 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 20.6 | 20.6 | 20.2 | 19.6 | 20.3 | 19.4 | 19.4 |
| 880 | 21.8 | 21.9 | 22.1 | 20.0 | 20.6 | 20.2 | 20.2 |
| MEAN | 21.8 | 21.6 | 21.2 | 20.7 | 21.4 | 20.5 | 20.6 |
| SD | 0.84 | 0.83 | 0.79 | 0.86 | 1.17 | 0.78 | 1.22 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

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DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 098
ABBR: TMCH

SEX: FEMALE
UNITS: pg

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 21.5 | 22.5 | 21.4 | 21.9 | 22.0 | 20.8 | 20.1 |
| 902 | 21.2 | 21.2 | 21.1 | 20.2 | 21.3 | 20.1 | 20.0 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 21.7 | 21.5 | 20.7 | 21.2 | -- | 20.0 | 20.3 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 21.0 | 21.6 | 21.7 | 22.2 | 22.1 | 20.3 | 19.8 |
| 909 | 21.1 | 21.6 | 20.4 | 21.1 | 20.9 | 19.0 | 19.5 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 21.2 | 21.8 | 22.5 | -- | 20.5 | 19.5 | 19.5 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 21.8 | 22.9 | 21.6 | 22.2 | 22.3 | 21.2 | 20.9 |
| 916 | 21.8 | 23.0 | 22.6 | 22.1 | 22.5 | 20.7 | 20.9 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 22.8 | 21.5 | 21.5 | 21.6 | 21.0 | 20.9 | 20.3 |
| 919 | 21.9 | 21.8 | 21.6 | 21.0 | 21.7 | 19.6 | 19.7 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 21.6 | 21.9 | 21.5 | 21.5 | 21.6 | 20.2 | 20.1 |
| SD | 0.53 | 0.63 | 0.69 | 0.68 | 0.70 | 0.70 | 0.51 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 20.5 | 21.5 | 20.4 | 20.1 | 21.4 | 19.6 | 20.2 |
| 942 | 21.5 | 20.5 | 21.8 | 19.3 | 22.3 | 21.2 | 21.3 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 21.0 | 19.5 | 20.0 | 19.7 | 20.4 | 19.2 | 18.5 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 21.7 | 21.5 | 19.7 | 19.1 | 20.2 | 19.4 | 19.5 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 22.5 | 21.0 | 21.1 | 21.0 | 21.2 | 20.0 | 20.6 |
| 954 | 21.2 | 20.0 | 18.8 | 18.8 | 20.0 | 18.9 | 19.7 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 20.5 | 19.8 | 19.0 | 22.8 | 19.9 | -- | -- |
| 957 | 20.7 | 19.6 | 19.0 | 19.3 | 20.3 | 19.0 | 20.3 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 21.7 | 21.1 | 20.2 | 19.2 | 20.9 | 19.9 | 20.3 |
| 960 | 20.7 | 21.1 | 21.0 | 19.4 | 20.9 | 19.8 | 20.2 |
| MEAN | 21.2 | 20.6 | 20.1 | 19.9 | 20.8 | 19.7 | 20.1 |
| SD | 0.65 | 0.78 | 1.00 | 1.20 | 0.74 | 0.69 | 0.78 |
| N | 10 | 10 | 10 | 10 | 10 | 9 | 9 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemo. Conc.

STUDY ID: 098
ABBR: TMCHC

SEX: FEMALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 35.6 | 35.8 | 37.0 | 36.6 | 37.3 | 36.0 | 36.2 |
| 824 | 37.4 | 36.7 | 37.0 | -- | 38.3 | 37.3 | 37.7 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 36.9 | 35.9 | 37.8 | 35.2 | 34.3 | 37.2 | 38.3 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 37.4 | 36.1 | 36.4 | 37.1 | 37.9 | 36.2 | 36.4 |
| 831 | 36.1 | 36.2 | 36.4 | 37.2 | 37.6 | 36.2 | 36.6 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 37.0 | 37.1 | 37.4 | 37.9 | 37.4 | 36.5 | 37.4 |
| 835 | 37.3 | 36.4 | 38.7 | 37.4 | 36.8 | 35.5 | 36.4 |
| 836 | 36.2 | 36.5 | 36.8 | 37.8 | 36.9 | 36.6 | 36.2 |
| 837 | 37.0 | 36.0 | 37.1 | 36.8 | 37.7 | 36.9 | 37.6 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 37.3 | 37.1 | 38.0 | 37.9 | 37.1 | 37.1 | 37.6 |
| MEAN | 36.8 | 36.4 | 37.3 | 37.1 | 37.1 | 36.6 | 37.0 |
| SD | 0.63 | 0.47 | 0.73 | 0.85 | 1.09 | 0.58 | 0.76 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 861 | 36.1 | 36.5 | 36.3 | 37.3 | 37.4 | 36.6 | 36.2 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 35.9 | 36.2 | 37.6 | 35.6 | 35.1 | 35.9 | 36.5 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 35.6 | 35.7 | 36.9 | 36.9 | 37.0 | 36.4 | 36.4 |
| 868 | 37.3 | 36.3 | 36.8 | 36.4 | -- | 34.1 | 36.6 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 36.6 | 36.4 | 36.7 | 36.6 | 39.5 | 35.8 | 36.4 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 36.2 | 36.0 | 36.2 | 36.7 | 37.0 | 35.9 | 35.9 |
| 874 | 36.7 | 35.7 | 36.3 | 37.4 | 37.3 | 36.0 | 36.6 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 37.6 | 36.4 | 36.6 | 36.9 | 37.6 | 36.4 | 36.1 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 36.8 | 35.9 | 36.3 | 36.1 | 36.8 | 35.7 | 36.4 |
| 880 | 36.8 | 37.3 | 38.1 | 36.9 | 36.7 | 36.4 | 37.1 |
| MEAN | 36.6 | 36.2 | 36.8 | 36.7 | 37.2 | 35.9 | 36.4 |
| SD | 0.62 | 0.47 | 0.62 | 0.54 | 1.14 | 0.71 | 0.33 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Mean Corpuscular Hemo. Conc.

STUDY ID: 098
ABBR: TMCHC

SEX: FEMALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 36.6 | 37.4 | 36.3 | 38.1 | 37.5 | 37.6 | 37.0 |
| 902 | 35.7 | 35.7 | 35.6 | 35.8 | 37.3 | 35.8 | 36.0 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 37.2 | 36.6 | 36.5 | 36.9 | -- | 36.6 | 37.1 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 36.7 | 36.4 | 37.4 | 37.9 | 37.0 | 36.6 | 36.7 |
| 909 | 37.3 | 36.9 | 35.9 | 37.0 | 36.9 | 35.4 | 36.4 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 35.7 | 36.6 | 38.0 | -- | 37.3 | 35.4 | 36.4 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 36.6 | 37.4 | 37.2 | 37.6 | 37.6 | 37.6 | 37.1 |
| 916 | 36.2 | 36.8 | 37.4 | 36.1 | 37.4 | 35.3 | 36.1 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 37.3 | 35.0 | 35.8 | 36.8 | 34.8 | 36.5 | 36.3 |
| 919 | 37.3 | 36.5 | 37.4 | 36.2 | 36.4 | 35.2 | 35.7 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 36.7 | 36.5 | 36.8 | 36.9 | 36.9 | 36.2 | 36.5 |
| SD | 0.63 | 0.73 | 0.83 | 0.81 | 0.87 | 0.92 | 0.48 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 34.5 | 35.1 | 36.0 | 35.4 | 36.0 | 36.5 | 37.0 |
| 942 | 36.6 | 34.3 | 38.7 | 32.8 | 36.6 | 38.0 | 37.7 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 36.4 | 34.8 | 37.2 | 38.0 | 37.6 | 37.5 | 35.7 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 36.3 | 35.6 | 35.7 | 36.0 | 36.2 | 36.7 | 36.9 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 37.5 | 34.6 | 36.6 | 36.1 | 35.4 | 35.8 | 35.9 |
| 954 | 36.4 | 34.4 | 34.6 | 36.1 | 35.5 | 35.8 | 36.5 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 35.5 | 35.2 | 35.6 | 44.0 | 36.0 | -- | -- |
| 957 | 35.9 | 34.2 | 35.8 | 36.4 | 36.4 | 36.1 | 36.9 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 36.5 | 35.7 | 36.7 | 35.6 | 37.0 | 37.0 | 37.5 |
| 960 | 36.3 | 35.1 | 37.2 | 35.8 | 37.5 | 36.6 | 36.8 |
| MEAN | 36.2 | 34.9 | 36.4 | 36.6 | 36.4 | 36.7 | 36.8 |
| SD | 0.78 | 0.53 | 1.13 | 2.89 | 0.76 | 0.74 | 0.66 |
| N | 10 | 10 | 10 | 10 | 10 | 9 | 9 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes Count

STUDY ID: 098
ABBR: RETICS

SEX: FEMALE
UNITS: % RBCs

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 0.3 | 1.3 | 0.7 | 0.7 | 0.4 | 0.0 | 0.5 |
| 824 | 1.3 | 1.5 | 0.5 | -- | 0.3 | 0.8 | 0.3 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 0.9 | 1.4 | 0.3 | 1.3 | 0.7 | 0.3 | 0.3 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 1.2 | 1.9 | 0.4 | 1.1 | 0.4 | 0.3 | 0.9 |
| 831 | 1.3 | 1.2 | 0.4 | 0.7 | 0.7 | 0.5 | 1.1 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 1.0 | 0.1 | 0.1 | 0.8 | 0.1 | 0.0 | 0.0 |
| 835 | 1.4 | 0.5 | 0.1 | 0.6 | 1.1 | 0.5 | 0.8 |
| 836 | 2.9 | 0.4 | 0.3 | 0.7 | 0.7 | 0.2 | 0.5 |
| 837 | 0.4 | 0.7 | 0.7 | 0.4 | 1.0 | 0.3 | 0.9 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 1.5 | 0.7 | 0.6 | 1.1 | 0.5 | 0.4 | 0.3 |
| MEAN | 1.2 | 1.0 | 0.4 | 0.8 | 0.6 | 0.3 | 0.6 |
| SD | 0.72 | 0.57 | 0.22 | 0.29 | 0.31 | 0.24 | 0.35 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 861 | 2.1 | 0.1 | 0.8 | 0.6 | 0.2 | 0.1 | 0.0 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 1.9 | 1.0 | 0.9 | 0.5 | 0.3 | 0.2 | 0.9 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 2.0 | 0.8 | 0.4 | 0.4 | 0.4 | 0.9 | 0.1 |
| 868 | 0.1 | 1.5 | 0.3 | 0.6 | -- | 0.8 | 0.3 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 0.7 | 0.6 | 0.4 | 0.8 | 0.1 | 0.8 | 0.8 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 0.7 | 0.6 | 0.6 | 1.4 | 1.5 | 0.5 | 1.9 |
| 874 | 1.2 | 1.1 | 0.5 | 0.6 | 0.7 | 0.2 | 0.3 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 0.6 | 1.8 | 0.8 | 0.9 | 0.5 | 0.1 | 0.1 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 1.1 | 1.0 | 0.4 | 0.7 | 1.0 | 0.1 | 0.7 |
| 880 | 1.3 | 1.6 | 1.0 | 0.9 | 0.1 | 0.3 | 0.6 |
| MEAN | 1.2 | 1.0 | 0.6 | 0.7 | 0.5 | 0.4 | 0.6 |
| SD | 0.67 | 0.52 | 0.25 | 0.28 | 0.47 | 0.32 | 0.56 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Reticulocytes Count

STUDY ID: 098
ABBR: RETICS

SEX: FEMALE
UNITS: % RBCs

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 0.1 | 1.9 | 0.4 | 0.9 | 0.7 | 0.5 | 0.5 |
| 902 | 0.0 | 2.2 | 1.7 | 1.7 | 0.8 | 0.3 | 0.0 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 0.1 | 0.3 | 1.0 | 0.9 | -- | 0.0 | 0.1 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 1.3 | 2.0 | 1.2 | 0.3 | 0.8 | 0.7 | 0.3 |
| 909 | 1.5 | 1.2 | 1.2 | 1.1 | 0.0 | 0.3 | 0.3 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 0.1 | 0.1 | 0.8 | -- | 0.8 | 0.2 | 0.2 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 0.3 | 1.7 | 0.5 | 0.9 | 1.3 | 0.4 | 0.7 |
| 916 | 1.1 | 2.1 | 1.2 | 0.6 | 0.3 | 0.6 | 0.0 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 0.9 | 2.9 | 0.9 | 1.2 | 1.2 | 0.3 | 0.6 |
| 919 | 1.1 | 0.2 | 1.3 | 0.2 | 0.1 | 0.2 | 0.6 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 0.7 | 1.5 | 1.0 | 0.9 | 0.7 | 0.4 | 0.3 |
| SD | 0.58 | 0.97 | 0.39 | 0.46 | 0.45 | 0.21 | 0.26 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 5.0 | 1.5 | 2.0 | 4.7 | 0.2 | 0.6 | 1.0 |
| 942 | 2.8 | 5.0 | 1.1 | CL | 1.9 | 0.2 | 0.2 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 2.7 | 3.5 | 1.2 | 0.8 | 1.4 | 0.0 | 0.1 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 4.2 | 0.5 | 1.5 | 3.7 | 0.9 | 0.2 | 0.4 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 4.2 | 2.5 | 2.2 | 1.5 | 0.6 | 0.4 | 0.5 |
| 954 | 3.6 | 2.1 | 1.2 | 2.8 | 0.9 | 0.2 | 0.4 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 3.9 | 1.4 | 2.0 | 3.0 | 0.9 | -- | -- |
| 957 | 3.8 | 2.0 | 1.6 | 0.5 | 0.9 | 0.2 | 0.3 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 0.4 | 0.7 | 1.1 | 1.8 | 0.3 | 0.5 | 0.7 |
| 960 | 4.1 | 3.0 | 2.1 | 4.6 | 0.5 | 0.3 | 1.2 |
| MEAN | 3.5 | 2.2 | 1.6 | 2.6 | 0.9 | 0.3 | 0.5 |
| SD | 1.27 | 1.36 | 0.44 | 1.55 | 0.51 | 0.18 | 0.37 |
| N | 10 | 10 | 10 | 9 | 10 | 9 | 9 |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: 098
ABBR: NRBC

SEX: FEMALE
UNITS: COUNT

ANIMAL ID Week 2 Week 4 Week 8 Week 13 Week 16 Week 21 Week 27

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 824 | 0 | 0 | 0 | -- | 0 | 0 | 0 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 831 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 835 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 836 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 837 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MEAN | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SD | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|
| 861 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 868 | 0 | 0 | 0 | 0 | -- | 0 | 0 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 874 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 880 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MEAN | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SD | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: 098
ABBR: NRBC

SEX: FEMALE
UNITS: COUNT

ANIMAL IO Week 2 Week 4 Week 8 Week 13 Week 16 Week 21 Week 27

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|
| 901 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| 902 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 0 | 0 | 0 | 0 | -- | 0 | 0 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 909 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 0 | 0 | 0 | -- | 0 | 0 | 0 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 916 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 919 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SO | 0.0 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|-----|-----|-----|-----|-----|-----|-----|
| 941 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| 942 | 0 | 0 | 0 | -- | 0 | 0 | 0 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 954 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 0 | 0 | 0 | 0 | 0 | -- | -- |
| 957 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 960 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MEAN | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SO | 0.3 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 |
| N | 10 | 10 | 10 | 9 | 10 | 9 | 9 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY 10: 098
ABBR: HB

SEX: FEMALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 824 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 831 | 0.0 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 0.0 | 0.5 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 |
| 835 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 836 | 0.0 | 0.0 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 |
| 837 | 0.0 | 0.0 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.16 | 0.20 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 861 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 0.2 | 0.0 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 |
| 868 | 0.0 | 0.0 | 0.0 | 0.1 | -- | 0.0 | 0.0 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 |
| 874 | 0.0 | 0.9 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 0.0 | 0.3 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 0.0 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 |
| 880 | 0.0 | 0.4 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.06 | 0.30 | 0.15 | 0.04 | 0.00 | 0.00 | 0.06 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Heinz Bodies

STUDY 10: 098
ABBR: HB

SEX: FEMALE
UNITS: %

| ANIMAL 10 | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 0.0 | 0.0 | 0.0 | 0.7 | 0.0 | 0.0 | 0.0 |
| 902 | 0.0 | 0.5 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 0.2 | 0.1 | 0.0 | 0.1 | -- | 0.0 | 0.0 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 0.1 | 0.0 | 0.5 | 0.0 | 0.0 | 0.0 | 0.0 |
| 909 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 0.0 | 1.1 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 916 | 0.2 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 0.0 | 1.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 919 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 0.1 | 0.3 | 0.1 | 0.1 | 0.0 | 0.0 | 0.0 |
| SD | 0.13 | 0.43 | 0.18 | 0.23 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 0.9 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 942 | 1.7 | 0.1 | 0.1 | CL | 0.0 | 0.0 | 0.0 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 0.8 | 1.3 | 0.2 | 0.1 | 0.0 | 0.0 | 0.0 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 1.4 | 0.2 | 0.2 | 0.7 | 0.0 | 0.0 | 0.0 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 1.9 | 0.4 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 |
| 954 | 1.0 | 0.7 | 0.3 | 1.9 | 0.0 | 0.0 | 0.0 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 2.8 | 0.5 | 1.3 | 1.1 | 0.0 | -- | -- |
| 957 | 1.9 | 0.3 | 0.1 | 1.0 | 0.0 | 0.0 | 0.0 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 0.8 | 0.0 | 0.0 | 1.1 | 0.0 | 0.0 | 0.0 |
| 960 | 3.7 | 0.3 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 |
| MEAN | 1.7 | 0.4 | 0.2 | 0.7 | 0.0 | 0.0 | 0.0 |
| SD | 0.95 | 0.39 | 0.39 | 0.63 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 10 | 9 | 9 |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: 098
ABBR: %METHGB

SEX: FEMALE
UNITS: %

ANIMAL ID Week 2 Week 4 Week 8 Week 13 Week 16 Week 21 Week 27

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 0.5 | 0.7 | 0.6 | 0.0 | 0.4 | 0.5 | 0.9 |
| 824 | 0.4 | 0.2 | 1.0 | -- | 0.0 | 0.5 | 0.3 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 0.7 | 0.6 | 0.9 | 0.1 | 0.5 | 0.6 | 0.8 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 0.7 | 0.2 | 0.6 | 0.1 | 0.5 | 0.8 | 0.7 |
| 831 | 0.2 | 0.3 | 0.7 | 1.2 | 0.0 | 0.1 | 0.5 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 0.4 | 0.4 | 0.1 | 1.7 | 1.1 | 1.0 | 0.6 |
| 835 | 0.1 | 0.2 | 1.1 | 0.7 | 0.4 | 0.5 | 0.7 |
| 836 | 0.5 | 1.0 | 0.5 | 0.1 | 0.3 | 0.6 | 1.3 |
| 837 | 1.1 | 0.7 | 0.5 | 0.8 | 1.5 | 0.9 | 0.8 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 0.1 | 0.4 | 0.7 | 1.0 | 0.2 | 0.6 | 0.8 |
| MEAN | 0.5 | 0.5 | 0.7 | 0.6 | 0.5 | 0.6 | 0.7 |
| SD | 0.31 | 0.27 | 0.29 | 0.60 | 0.47 | 0.25 | 0.26 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 861 | 1.1 | 0.4 | 1.2 | 0.6 | 0.0 | 0.8 | 1.0 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 0.4 | 0.6 | 0.0 | 0.8 | 0.2 | 0.8 | 0.5 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 0.4 | 0.4 | 0.9 | 0.5 | 0.0 | 0.7 | 0.7 |
| 868 | 0.2 | 0.0 | 0.3 | 0.0 | -- | 0.8 | 1.0 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 0.7 | 0.2 | 0.5 | 0.6 | 0.2 | 0.3 | 0.8 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 0.2 | 1.4 | 0.6 | 0.7 | 0.5 | 0.7 | 0.7 |
| 874 | 0.2 | 0.7 | 1.0 | 0.4 | 0.6 | 0.4 | 0.9 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 0.8 | 1.0 | 0.6 | 0.5 | 0.2 | 0.2 | 0.9 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 0.1 | 1.0 | 0.3 | 1.1 | 0.5 | 0.3 | 1.3 |
| 880 | 0.9 | 0.7 | 0.1 | 0.4 | 0.2 | 0.3 | 1.6 |
| MEAN | 0.5 | 0.6 | 0.6 | 0.6 | 0.3 | 0.5 | 0.9 |
| SD | 0.35 | 0.42 | 0.39 | 0.29 | 0.22 | 0.25 | 0.32 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: 098
ABBR: %METHGB

SEX: FEMALE
UNITS: %

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 0.5 | 2.1 | 4.2 | 4.7 | 0.1 | 1.4 | 0.6 |
| 902 | 0.7 | 2.9 | 5.0 | 6.4 | 0.3 | 0.3 | 1.1 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 1.3 | 3.7 | 6.1 | 6.5 | -- | 0.5 | 0.4 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 0.8 | 3.5 | 4.7 | 5.5 | 0.0 | 0.2 | 0.4 |
| 909 | 0.4 | 3.1 | 3.3 | 3.6 | 0.0 | 0.1 | 0.9 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 0.7 | 2.0 | 2.8 | -- | 0.5 | 0.9 | 1.2 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 0.7 | 1.4 | 3.0 | 3.1 | 0.9 | 0.4 | 1.2 |
| 916 | 1.8 | 1.9 | 3.5 | 2.3 | 0.0 | 0.9 | 0.8 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 0.6 | 2.1 | 4.4 | 5.3 | 1.7 | 0.8 | 0.6 |
| 919 | 1.1 | 2.6 | 4.9 | 5.0 | 0.0 | 1.0 | 0.6 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 0.9 | 2.5 | 4.2 | 4.7 | 0.4 | 0.7 | 0.8 |
| SD | 0.42 | 0.75 | 1.04 | 1.45 | 0.58 | 0.41 | 0.31 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 10.1 | 5.8 | 6.1 | 7.8 | 0.1 | 1.0 | 0.6 |
| 942 | 15.9 | 6.1 | 6.6 | 13.4 | 1.6 | 0.8 | 0.1 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 11.2 | 7.5 | 6.8 | 9.8 | 0.0 | 0.2 | 0.2 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 13.9 | 8.4 | 9.0 | 11.3 | 1.0 | 0.6 | 1.2 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 12.4 | 7.5 | 9.6 | 11.7 | 1.2 | 0.5 | 0.7 |
| 954 | 15.0 | 9.8 | 10.7 | 16.3 | 2.0 | 0.7 | 0.8 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 12.9 | 10.6 | 10.3 | 11.8 | 1.7 | -- | -- |
| 957 | 10.5 | 6.6 | 10.1 | 12.8 | 2.2 | 0.7 | 0.1 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 14.6 | 11.5 | 14.2 | 15.9 | 2.1 | 0.9 | 1.3 |
| 960 | 12.4 | 6.8 | 8.9 | 11.3 | 2.0 | 1.1 | 0.9 |
| MEAN | 12.9 | 8.1 | 9.2 | 12.2 | 1.4 | 0.7 | 0.7 |
| SD | 1.95 | 1.96 | 2.40 | 2.57 | 0.80 | 0.27 | 0.45 |
| N | 10 | 10 | 10 | 10 | 10 | 9 | 9 |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: 098
ABBR: PLT

SEX: FEMALE
UNITS: 10³/ccm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 919 | 1099 | 1118 | 1069 | 990 | 964 | 1015 |
| 824 | 1287 | 1140 | 1064 | -- | 913 | 919 | 963 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 1190 | 1022 | 682 | 979 | 1002 | 959 | 1092 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 1224 | 1240 | 818 | 1039 | 1145 | 998 | 1109 |
| 831 | 1440 | 1271 | 1187 | 1156 | 1075 | 1105 | 985 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 1280 | 1227 | 1127 | 867 | 1037 | 990 | 1034 |
| 835 | 1263 | 1188 | 1104 | 910 | 957 | 1020 | 979 |
| 836 | 1189 | 1143 | 1050 | 795 | 885 | 872 | 966 |
| 837 | 1117 | 1034 | 949 | 959 | 640 | 519 | 722 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 1262 | 1335 | 1199 | 1077 | 1030 | 1032 | 944 |
| MEAN | 1217 | 1170 | 1030 | 983 | 967 | 938 | 981 |
| SD | 134.6 | 101.6 | 166.7 | 114.0 | 137.7 | 160.3 | 106.3 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|-------|-------|-------|-------|-------|-------|-------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 861 | 1118 | 1071 | 990 | 844 | 912 | 918 | 813 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 1251 | 1184 | 1066 | 1032 | 1000 | 905 | 950 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 1345 | 1392 | 1112 | 992 | 993 | 1112 | 1022 |
| 868 | 1050 | 1127 | 905 | 833 | -- | 400 | 955 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 1325 | 1221 | 1184 | 1301 | 1157 | 1216 | 1220 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 1280 | 1229 | 1151 | 1141 | 1056 | 1061 | 1070 |
| 874 | 1448 | 1375 | 1227 | 1027 | 1118 | 1045 | 1089 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 1171 | 787 | 1053 | 967 | 944 | 974 | 982 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 1433 | 1496 | 1250 | 1246 | 1340 | 1266 | 1165 |
| 880 | 1632 | 1438 | 1222 | 1310 | 769 | 1142 | 1007 |
| MEAN | 1305 | 1232 | 1116 | 1069 | 1032 | 1004 | 1027 |
| SD | 172.3 | 209.7 | 112.7 | 174.5 | 162.9 | 243.2 | 116.1 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Platelets

STUDY ID: 098
ABBR: PLT

SEX: FEMALE
UNITS: 10³/ccn

ANIMAL ID Week 2 Week 4 Week 8 Week 13 Week 16 Week 21 Week 27

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|------|-------|------|------|-------|-------|-------|------|
| 901 | 1176 | 1128 | 1029 | 889 | 1062 | 1071 | 1113 |
| 902 | 1176 | 1208 | 1037 | 1040 | 1004 | 954 | 983 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 1457 | 1393 | 1264 | 1271 | -- | 1218 | 1165 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 1628 | 1294 | 1082 | 1303 | 1057 | 1048 | 1075 |
| 909 | 1205 | 1119 | 1004 | 840 | 1003 | 1011 | 997 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 1058 | 1258 | 990 | -- | 928 | 736 | 1000 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 1172 | 1201 | 1047 | 1153 | 1120 | 1092 | 940 |
| 916 | 1370 | 1245 | 1206 | 1170 | 815 | 1098 | 1046 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 1304 | 1250 | 1025 | 1035 | 727 | 998 | 982 |
| 919 | 997 | 1113 | 1039 | 997 | 1059 | 942 | 970 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 1254 | 1221 | 1072 | 1078 | 975 | 1017 | 1027 |
| SD | 189.4 | 87.5 | 90.2 | 159.8 | 129.1 | 127.1 | 71.1 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|------|-------|-------|-------|-------|-------|-------|-------|
| 941 | 1199 | 1228 | 950 | 920 | 887 | 1064 | 935 |
| 942 | 828 | 823 | 868 | 246 | 833 | 969 | 895 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 1535 | 1329 | 1253 | 1280 | 1208 | 1163 | 1123 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 1279 | 1209 | 1013 | 854 | 984 | 877 | 834 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 1482 | 1382 | 1140 | 805 | 1017 | 1012 | 909 |
| 954 | 1115 | 1063 | 735 | 722 | 859 | 819 | 795 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 1315 | 1230 | 1093 | 804 | 1049 | -- | -- |
| 957 | 1815 | 1243 | 1202 | 1070 | 1098 | 1010 | 1013 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 1279 | 1335 | 1225 | 1169 | 1210 | 1086 | 1051 |
| 960 | 954 | 921 | 981 | 848 | 810 | 742 | 830 |
| MEAN | 1280 | 1176 | 1046 | 872 | 996 | 971 | 932 |
| SD | 286.3 | 184.0 | 167.7 | 283.0 | 147.7 | 135.2 | 110.6 |
| N | 10 | 10 | 10 | 10 | 10 | 9 | 9 |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATSINDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. TimeSTUDY ID: 098
ABBR: APTTSEX: FEMALE
UNITS: sec

ANIMAL ID Week 14 Week 27

GROUP: 0:0 mg base/kg/day

| | | |
|-----|------|------|
| 821 | 14.5 | -- |
| 822 | 14.7 | -- |
| 823 | -- | 15.6 |
| 824 | -- | 11.8 |
| 825 | 15.2 | -- |
| 826 | 17.3 | -- |
| 827 | -- | 12.8 |
| 828 | 16.5 | -- |
| 829 | 11.7 | -- |
| 830 | -- | 10.0 |
| 831 | -- | 12.8 |
| 832 | 15.7 | -- |
| 833 | 13.5 | -- |
| 834 | -- | 13.8 |
| 835 | -- | 15.5 |
| 836 | -- | 14.2 |
| 837 | -- | 11.1 |
| 838 | 17.1 | -- |
| 839 | 18.9 | -- |
| 840 | -- | 10.0 |

| | | |
|------|------|------|
| MEAN | 15.5 | 12.8 |
| SD | 2.07 | 2.05 |
| N | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | |
|-----|------|------|
| 861 | -- | 15.3 |
| 862 | 16.3 | -- |
| 863 | 16.0 | -- |
| 864 | -- | 16.4 |
| 865 | 17.5 | -- |
| 866 | 14.2 | -- |
| 867 | -- | 15.0 |
| 868 | -- | 13.1 |
| 869 | 15.2 | -- |
| 870 | 11.2 | -- |
| 871 | -- | 10.4 |
| 872 | 11.7 | -- |
| 873 | -- | 12.8 |
| 874 | -- | 8.2 |
| 875 | 15.4 | -- |
| 876 | 14.2 | -- |
| 877 | -- | 15.1 |
| 878 | 14.1 | -- |
| 879 | -- | 12.3 |
| 880 | -- | 16.1 |

| | | |
|------|------|------|
| MEAN | 14.6 | 13.5 |
| SD | 1.97 | 2.65 |
| N | 10 | 10 |

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Act. Partial Thrombo. Time

STUDY ID: 098
ABBR: APTT

SEX: FEMALE
UNITS: sec

ANIMAL ID Week 14 Week 27

GROUP: 6.0:6.0 mg base/kg/day

| | | |
|-----|------|------|
| 901 | -- | 18.0 |
| 902 | -- | 11.9 |
| 903 | 13.5 | -- |
| 904 | -- | 12.5 |
| 905 | 16.2 | -- |
| 906 | 13.0 | -- |
| 907 | 9.0 | -- |
| 908 | -- | 13.9 |
| 909 | -- | 14.1 |
| 910 | 12.4 | -- |
| 911 | 10.7 | -- |
| 912 | -- | 8.5 |
| 913 | 15.7 | -- |
| 914 | 15.1 | -- |
| 915 | -- | 13.1 |
| 916 | -- | 16.9 |
| 917 | 15.7 | -- |
| 918 | -- | 14.9 |
| 919 | -- | 13.2 |
| 920 | 14.7 | -- |

| | | |
|------|------|------|
| MEAN | 13.6 | 13.7 |
| SD | 2.37 | 2.64 |
| N | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | |
|-----|------|------|
| 941 | -- | 15.2 |
| 942 | -- | 15.3 |
| 943 | 13.1 | -- |
| 944 | -- | 15.8 |
| 945 | 12.4 | -- |
| 946 | 11.3 | -- |
| 947 | 15.7 | -- |
| 948 | 8.5 | -- |
| 949 | -- | 18.3 |
| 950 | 7.2 | -- |
| 951 | 10.4 | -- |
| 952 | 13.2 | -- |
| 953 | -- | 14.6 |
| 954 | -- | 16.2 |
| 955 | 18.4 | -- |
| 956 | -- | -- |
| 957 | -- | 16.6 |
| 958 | 12.5 | -- |
| 959 | -- | 11.6 |
| 960 | -- | 14.2 |

| | | |
|------|------|------|
| MEAN | 12.3 | 15.3 |
| SD | 3.25 | 1.84 |
| N | 10 | 9 |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY IO: 098
ABBR: WBC

SEX: FEMALE
UNITS: 10³/cmm

| ANIMAL IO | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 12.6 | 7.0 | 8.5 | 9.8 | 6.1 | 7.4 | 7.7 |
| 824 | 12.9 | 10.4 | 6.5 | -- | 5.7 | 5.5 | 8.1 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 17.5 | 14.2 | 9.4 | 10.0 | 9.0 | 11.9 | 10.9 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 17.9 | 11.2 | 8.8 | 10.0 | 7.9 | 8.9 | 8.2 |
| 831 | 21.6 | 16.3 | 15.4 | 14.2 | 15.9 | 13.6 | 10.7 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 13.1 | 15.1 | 13.4 | 12.5 | 9.0 | 10.2 | 8.3 |
| 835 | 11.1 | 9.0 | 8.4 | 8.6 | 7.8 | 9.8 | 7.8 |
| 836 | 17.8 | 9.5 | 11.7 | 10.1 | 9.9 | 8.8 | 9.4 |
| 837 | 16.7 | 10.4 | 10.7 | 8.4 | 8.4 | 7.5 | 9.6 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 15.4 | 12.6 | 11.4 | 12.3 | 10.1 | 9.5 | 10.8 |
| MEAN | 15.7 | 11.6 | 10.4 | 10.7 | 9.0 | 9.3 | 9.2 |
| SD | 3.23 | 2.93 | 2.65 | 1.93 | 2.83 | 2.31 | 1.30 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 861 | 13.1 | 11.1 | 14.5 | 9.6 | 10.0 | 11.2 | 6.9 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 18.9 | 21.4 | 20.0 | 12.8 | 11.0 | 11.6 | 11.7 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 19.4 | 14.1 | 10.3 | 10.2 | 10.5 | 9.1 | 9.5 |
| 868 | 16.6 | 18.5 | 14.8 | 9.4 | -- | 6.9 | 8.9 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 19.7 | 11.4 | 14.7 | 12.1 | 12.0 | 10.8 | 12.6 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 11.2 | 11.9 | 12.6 | 10.2 | 10.2 | 11.0 | 10.3 |
| 874 | 14.0 | 17.0 | 12.9 | 12.0 | 9.3 | 8.9 | 6.8 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 16.5 | 13.9 | 10.2 | 9.6 | 10.1 | 10.2 | 8.6 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 17.6 | 18.8 | 12.6 | 12.0 | 11.8 | 9.2 | 9.6 |
| 880 | 29.0 | 16.4 | 13.2 | 14.0 | 12.4 | 12.1 | 10.9 |
| MEAN | 17.6 | 15.5 | 13.6 | 11.2 | 10.8 | 10.1 | 9.6 |
| SD | 4.90 | 3.52 | 2.78 | 1.59 | 1.05 | 1.57 | 1.89 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Leukocytes

STUDY ID: 098
ABBR: WBC

SEX: FEMALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 17.4 | 14.2 | 25.0 | 17.2 | 10.3 | 11.0 | 11.7 |
| 902 | 14.1 | 11.1 | 11.8 | 16.3 | 5.8 | 6.0 | 8.1 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 18.9 | 19.4 | 17.5 | 14.1 | -- | 10.0 | 7.3 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 13.9 | 12.5 | 10.9 | 10.7 | 7.5 | 7.3 | 8.6 |
| 909 | 12.5 | 12.7 | 10.0 | 8.7 | 7.3 | 9.8 | 8.5 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 18.8 | 29.9 | 21.8 | -- | 14.4 | 9.5 | 11.4 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 22.7 | 16.6 | 17.8 | 14.4 | 10.8 | 10.0 | 11.0 |
| 916 | 16.9 | 12.3 | 12.7 | 11.1 | 9.6 | 11.2 | 9.8 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 21.2 | 23.6 | 18.9 | 20.6 | 8.8 | 12.6 | 13.9 |
| 919 | 17.4 | 19.9 | 15.4 | 12.6 | 8.7 | 8.1 | 9.8 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 17.4 | 17.2 | 16.2 | 14.0 | 9.2 | 9.6 | 10.0 |
| SD | 3.23 | 6.03 | 4.93 | 3.68 | 2.49 | 1.95 | 2.01 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 28.3 | 17.1 | 23.0 | 14.1 | 10.9 | 9.6 | 9.6 |
| 942 | 20.8 | 19.1 | 14.6 | 19.8 | 9.0 | 11.4 | 7.5 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 23.3 | 15.3 | 17.9 | 20.2 | 14.4 | 11.6 | 10.3 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 32.4 | 31.1 | 30.2 | 31.1 | 19.4 | 11.1 | 13.1 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 32.5 | 24.0 | 25.3 | 18.5 | 13.0 | 13.8 | 7.4 |
| 954 | 24.9 | 20.9 | 20.9 | 23.0 | 10.3 | 8.8 | 9.5 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 17.9 | 17.6 | 24.5 | 29.4 | 10.1 | -- | -- |
| 957 | 23.5 | 25.7 | 18.9 | 22.3 | 14.7 | 10.7 | 9.1 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 19.1 | 17.4 | 21.3 | 24.3 | 13.9 | 10.2 | 8.5 |
| 960 | 34.9 | 27.2 | 27.0 | 27.7 | 13.4 | 9.6 | 7.5 |
| MEAN | 25.8 | 21.5 | 22.4 | 23.0 | 12.9 | 10.8 | 9.2 |
| SD | 5.98 | 5.21 | 4.62 | 5.25 | 3.03 | 1.47 | 1.81 |
| N | 10 | 10 | 10 | 10 | 10 | 9 | 9 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: M. Neutrophils

STUDY ID: 098
ABBR: M. Neutrop

SEX: FEMALE
UNITS: 10³/cmn

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 0.9 | 1.6 | 1.1 | 1.8 | 1.2 | 1.5 | 1.6 |
| 824 | 1.2 | 1.0 | 0.9 | -- | 1.1 | 0.9 | 2.0 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 2.8 | 1.6 | 1.0 | 1.1 | 1.6 | 2.4 | 4.7 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 2.7 | 1.0 | 1.6 | 2.0 | 1.2 | 2.1 | 1.3 |
| 831 | 2.4 | 1.6 | 2.3 | 3.7 | 3.0 | 1.5 | 1.2 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 1.3 | 0.6 | 1.1 | 2.6 | 0.7 | 1.3 | 0.4 |
| 835 | 1.4 | 0.9 | 0.3 | 1.9 | 0.8 | 1.0 | 0.8 |
| 836 | 3.7 | 1.6 | 3.2 | 1.8 | 1.6 | 1.3 | 1.3 |
| 837 | 2.3 | 0.9 | 1.3 | 1.2 | 0.8 | 1.0 | 0.0 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 2.5 | 2.0 | 1.0 | 1.0 | 0.7 | 0.8 | 2.2 |
| MEAN | 2.1 | 1.3 | 1.4 | 1.9 | 1.3 | 1.4 | 1.6 |
| SD | 0.89 | 0.45 | 0.82 | 0.84 | 0.69 | 0.52 | 1.29 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 861 | 2.2 | 1.3 | 1.7 | 1.2 | 3.7 | 1.8 | 0.7 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 3.8 | 2.8 | 1.2 | 0.9 | 2.2 | 1.6 | 4.0 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 1.6 | 1.0 | 1.9 | 0.6 | 0.7 | 1.0 | 0.6 |
| 868 | 0.7 | 1.3 | 2.2 | 0.7 | -- | 0.6 | 1.1 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 3.2 | 0.7 | 1.6 | 1.5 | 2.5 | 1.0 | 2.4 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 1.3 | 1.9 | 1.3 | 0.1 | 0.7 | 1.9 | 1.6 |
| 874 | 0.7 | 0.9 | 0.5 | 1.2 | 1.7 | 1.1 | 1.5 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 2.0 | 2.8 | 1.0 | 1.2 | 1.4 | 2.8 | 2.3 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 1.1 | 2.3 | 0.3 | 1.8 | 2.0 | 0.9 | 1.6 |
| 880 | 3.8 | 0.5 | 2.4 | 1.1 | 1.7 | 0.6 | 2.0 |
| MEAN | 2.0 | 1.6 | 1.4 | 1.0 | 1.8 | 1.3 | 1.8 |
| SD | 1.19 | 0.85 | 0.69 | 0.48 | 0.93 | 0.69 | 0.99 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: M. Neutrophils

STUDY ID: 098
ABBR: M. Neutrop

SEX: FEMALE
UNITS: 10³/cm³

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 1.0 | 1.4 | 5.5 | 1.7 | 1.9 | 0.9 | 1.3 |
| 902 | 3.4 | 1.3 | 2.1 | 2.8 | 0.6 | 1.1 | 2.6 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 2.5 | 3.9 | 1.8 | 2.5 | -- | 0.9 | 2.0 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 2.1 | 2.4 | 2.8 | 3.3 | 1.8 | 1.8 | 2.8 |
| 909 | 1.5 | 3.2 | 4.7 | 4.3 | 1.3 | 1.4 | 1.3 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 0.4 | 7.8 | 5.2 | -- | 3.7 | 1.3 | 1.5 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 4.8 | 2.5 | 5.2 | 3.3 | 2.6 | 2.3 | 2.3 |
| 916 | 1.9 | 2.2 | 1.1 | 2.8 | 1.8 | 0.2 | 1.5 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 2.3 | 3.3 | 3.6 | 2.5 | 3.0 | 0.9 | 1.1 |
| 919 | 2.8 | 3.0 | 2.8 | 3.0 | 0.9 | 1.1 | 1.3 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 2.3 | 3.1 | 3.5 | 2.9 | 2.0 | 1.2 | 1.8 |
| SD | 1.24 | 1.84 | 1.59 | 0.71 | 1.00 | 0.57 | 0.61 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 3.7 | 1.4 | 4.6 | 1.8 | 2.2 | 2.8 | 2.9 |
| 942 | 3.3 | 5.2 | 1.8 | -- | 2.5 | 3.6 | 2.1 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 4.9 | 2.1 | 2.1 | 2.6 | 3.5 | 1.7 | 0.9 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 6.5 | 4.0 | 2.7 | 4.7 | 4.1 | 1.2 | 1.7 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 5.2 | 2.9 | 2.0 | 3.1 | 2.0 | 1.4 | 0.9 |
| 954 | 4.5 | 5.2 | 1.7 | 4.8 | 1.6 | 1.6 | 0.5 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 3.4 | 3.0 | 2.7 | 2.9 | 1.4 | -- | -- |
| 957 | 6.1 | 4.1 | 1.7 | 3.8 | 2.6 | 1.3 | 1.8 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 4.6 | 2.8 | 3.0 | 4.9 | 2.6 | 2.0 | 2.0 |
| 960 | 5.2 | 1.6 | 2.2 | 1.9 | 2.5 | 1.9 | 1.0 |
| MEAN | 4.7 | 3.2 | 2.5 | 3.4 | 2.5 | 1.9 | 1.5 |
| SD | 1.08 | 1.36 | 0.88 | 1.22 | 0.81 | 0.78 | 0.76 |
| N | 10 | 10 | 10 | 9 | 10 | 9 | 9 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: I. Neutrophils

STUDY ID: 098
ABBR: I. Neutrop

SEX: FEMALE
UNITS: 10³/cm³

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 824 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 14.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 831 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 835 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 836 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 837 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 2.2 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 1.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 |
| SD | 4.49 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.70 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 861 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 868 | 0.0 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 0.0 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 874 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 880 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.03 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: I. Neutrophils

STUDY ID: 098
ABBR: I. Neutrop

SEX: FEMALE
UNITS: $10^3/\text{cm}^3$

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 902 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 0.0 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 909 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 916 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 18.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 919 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 1.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 5.76 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 942 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 954 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | -- | -- |
| 957 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 960 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 10 | 9 | 9 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Lymphocytes

STUDY ID: 098
ABBR: Lymphocyte

SEX: FEMALE
UNITS: 10³/cmn

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 11.3 | 5.2 | 6.3 | 7.6 | 4.8 | 5.6 | 5.2 |
| 824 | 9.8 | 8.5 | 5.1 | -- | 4.3 | 4.3 | 5.9 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 0.4 | 12.5 | 7.7 | 8.6 | 7.2 | 8.6 | 5.8 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 15.2 | 9.7 | 6.5 | 7.8 | 6.3 | 6.1 | 6.2 |
| 831 | 18.1 | 14.2 | 12.3 | 9.9 | 12.4 | 11.6 | 8.9 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 11.8 | 12.7 | 11.9 | 9.8 | 7.5 | 8.6 | 7.9 |
| 835 | 9.3 | 7.5 | 7.3 | 6.6 | 6.6 | 8.5 | 6.5 |
| 836 | 13.4 | 7.2 | 8.1 | 7.9 | 8.1 | 7.0 | 7.5 |
| 837 | 14.0 | 9.4 | 9.2 | 7.2 | 7.1 | 6.2 | 0.0 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 12.9 | 10.0 | 9.6 | 10.5 | 9.0 | 8.5 | 8.5 |
| MEAN | 11.6 | 9.7 | 8.4 | 8.4 | 7.3 | 7.5 | 6.2 |
| SD | 4.71 | 2.79 | 2.36 | 1.35 | 2.27 | 2.08 | 2.51 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 861 | 10.6 | 9.3 | 11.9 | 8.1 | 6.0 | 8.7 | 5.9 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 14.6 | 17.1 | 17.8 | 11.8 | 7.9 | 9.4 | 6.9 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 17.7 | 12.7 | 7.9 | 9.3 | 9.3 | 7.2 | 8.6 |
| 868 | 15.4 | 16.3 | 12.1 | 8.3 | -- | 6.1 | 7.6 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 16.5 | 10.6 | 11.9 | 9.7 | 8.8 | 9.4 | 9.8 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 9.6 | 9.6 | 10.7 | 9.9 | 9.1 | 8.5 | 8.0 |
| 874 | 13.2 | 15.5 | 11.6 | 10.6 | 6.7 | 7.7 | 5.1 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 13.9 | 10.6 | 8.8 | 8.3 | 8.6 | 7.3 | 5.8 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 16.5 | 15.8 | 11.6 | 9.2 | 9.4 | 8.0 | 7.3 |
| 880 | 25.2 | 15.3 | 10.7 | 12.6 | 10.3 | 11.3 | 8.4 |
| MEAN | 15.3 | 13.3 | 11.5 | 9.8 | 8.5 | 8.4 | 7.3 |
| SD | 4.32 | 3.04 | 2.62 | 1.51 | 1.37 | 1.46 | 1.45 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Lymphocytes

STUDY ID: 098
ABBR: Lymphocyte

SEX: FEMALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 15.3 | 12.4 | 18.8 | 14.3 | 8.0 | 9.5 | 9.8 |
| 902 | 10.6 | 9.1 | 9.3 | 12.4 | 4.8 | 4.6 | 5.3 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 15.7 | 15.5 | 15.8 | 11.6 | -- | 8.9 | 4.9 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 11.5 | 9.9 | 7.3 | 6.5 | 5.3 | 5.4 | 5.4 |
| 909 | 10.0 | 8.9 | 4.6 | 4.4 | 5.6 | 7.9 | 7.1 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 18.0 | 20.6 | 16.1 | -- | 9.6 | 7.7 | 8.4 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 17.7 | 13.3 | 11.9 | 10.1 | 7.6 | 6.9 | 8.1 |
| 916 | 14.4 | 9.8 | 10.3 | 7.8 | 7.5 | 10.3 | 7.5 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 0.6 | 19.4 | 14.6 | 17.5 | 5.8 | 11.6 | 12.5 |
| 919 | 14.4 | 16.5 | 11.4 | 9.2 | 7.2 | 6.9 | 8.3 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 12.8 | 13.5 | 12.0 | 10.4 | 6.8 | 8.0 | 7.7 |
| SD | 5.10 | 4.30 | 4.37 | 4.04 | 1.55 | 2.16 | 2.30 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 23.2 | 13.5 | 16.1 | 11.6 | 8.1 | 6.3 | 6.1 |
| 942 | 15.0 | 11.3 | 11.0 | -- | 6.1 | 7.0 | 4.7 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 16.3 | 12.4 | 14.0 | 14.5 | 10.7 | 9.5 | 8.7 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 24.6 | 24.6 | 26.6 | 21.8 | 13.8 | 9.0 | 10.7 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 25.7 | 18.7 | 15.2 | 13.0 | 10.7 | 11.7 | 6.1 |
| 954 | 18.4 | 13.4 | 16.9 | 14.5 | 8.5 | 7.0 | 8.5 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 13.1 | 12.3 | 18.4 | 22.9 | 8.4 | -- | -- |
| 957 | 15.5 | 16.7 | 14.9 | 17.6 | 11.3 | 9.3 | 6.9 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 13.6 | 12.9 | 15.5 | 15.8 | 11.0 | 7.7 | 5.9 |
| 960 | 26.2 | 22.6 | 21.9 | 22.7 | 10.2 | 7.0 | 6.5 |
| MEAN | 19.2 | 15.8 | 17.1 | 17.2 | 9.9 | 8.3 | 7.1 |
| SD | 5.22 | 4.67 | 4.39 | 4.32 | 2.15 | 1.73 | 1.84 |
| N | 10 | 10 | 10 | 9 | 10 | 9 | 9 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Monocytes

STUDY ID: 098
ABBR: Monocytes

SEX: FEMALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|---------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 0:0 mg base/kg/day | | | | | | | |
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 0.4 | 0.1 | 1.0 | 0.3 | 0.2 | 0.4 | 0.8 |
| 824 | 1.8 | 0.7 | 0.5 | -- | 0.2 | 0.1 | 0.2 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 0.2 | 0.1 | 0.7 | 0.2 | 0.2 | 0.7 | 0.3 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 0.0 | 0.3 | 0.6 | 0.1 | 0.2 | 0.5 | 0.6 |
| 831 | 0.6 | 0.5 | 0.6 | 0.6 | 0.5 | 0.4 | 0.5 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 0.0 | 1.5 | 0.3 | 0.1 | 0.8 | 0.3 | 0.0 |
| 835 | 0.2 | 0.5 | 0.8 | 0.1 | 0.4 | 0.2 | 0.5 |
| 836 | 0.5 | 0.5 | 0.2 | 0.3 | 0.2 | 0.4 | 0.5 |
| 837 | 0.0 | 0.0 | 0.2 | 0.0 | 0.4 | 0.2 | 7.1 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 0.0 | 0.5 | 0.6 | 0.6 | 0.0 | 0.2 | 0.1 |
| MEAN | 0.4 | 0.5 | 0.6 | 0.3 | 0.3 | 0.3 | 1.1 |
| SD | 0.55 | 0.43 | 0.26 | 0.22 | 0.22 | 0.18 | 2.14 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

| | | | | | | | |
|-------------------------------|------|------|------|------|------|------|------|
| GROUP: 0.5:0.5 mg base/kg/day | | | | | | | |
| 861 | 0.3 | 0.4 | 0.6 | 0.3 | 0.2 | 0.4 | 0.2 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 0.4 | 1.5 | 1.0 | 0.1 | 0.8 | 0.5 | 0.6 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 0.0 | 0.4 | 0.5 | 0.1 | 0.2 | 0.5 | 0.4 |
| 868 | 0.5 | 0.6 | 0.4 | 0.5 | -- | 0.2 | 0.0 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 0.0 | 0.0 | 0.7 | 1.0 | 0.5 | 0.4 | 0.4 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 0.2 | 0.4 | 0.6 | 0.2 | 0.2 | 0.6 | 0.6 |
| 874 | 0.1 | 0.7 | 0.6 | 0.0 | 0.7 | 0.2 | 0.1 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 0.3 | 0.6 | 0.1 | 0.1 | 0.0 | 0.1 | 0.4 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 0.0 | 0.2 | 0.3 | 0.5 | 0.2 | 0.1 | 0.6 |
| 880 | 0.0 | 0.2 | 0.1 | 0.1 | 0.2 | 0.2 | 0.4 |
| MEAN | 0.2 | 0.5 | 0.5 | 0.3 | 0.3 | 0.3 | 0.4 |
| SD | 0.19 | 0.41 | 0.28 | 0.30 | 0.27 | 0.18 | 0.21 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Monocytes

STUDY ID: 098
ABBR: Monocytes

SEX: FEMALE
UNITS: $10^3/\text{cmm}$

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 0.7 | 0.1 | 0.5 | 0.9 | 0.4 | 0.6 | 0.5 |
| 902 | 0.1 | 0.6 | 0.1 | 0.8 | 0.2 | 0.2 | 0.0 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 0.4 | 0.0 | 0.0 | 0.0 | -- | 0.1 | 0.2 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 0.3 | 0.1 | 0.7 | 0.5 | 0.4 | 0.1 | 0.4 |
| 909 | 0.9 | 0.5 | 0.5 | 0.0 | 0.2 | 0.3 | 0.2 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 0.2 | 1.5 | 0.2 | -- | 0.9 | 0.2 | 1.1 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 0.0 | 0.7 | 0.7 | 0.6 | 0.5 | 0.7 | 0.3 |
| 916 | 0.5 | 0.1 | 1.3 | 0.4 | 0.2 | 0.7 | 0.6 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 0.0 | 0.5 | 0.6 | 0.6 | 0.0 | 0.1 | 0.3 |
| 919 | 0.0 | 0.2 | 1.1 | 0.4 | 0.6 | 0.1 | 0.2 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 0.3 | 0.4 | 0.6 | 0.5 | 0.4 | 0.3 | 0.4 |
| SD | 0.31 | 0.45 | 0.41 | 0.31 | 0.27 | 0.26 | 0.30 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 1.4 | 2.1 | 2.3 | 0.6 | 0.3 | 0.4 | 0.4 |
| 942 | 2.5 | 2.7 | 1.8 | -- | 0.4 | 0.2 | 0.7 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 1.9 | 0.8 | 1.6 | 3.0 | 0.0 | 0.1 | 0.5 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 1.0 | 2.5 | 0.9 | 4.7 | 1.2 | 0.6 | 0.7 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 1.6 | 2.4 | 8.1 | 2.4 | 0.3 | 0.7 | 0.4 |
| 954 | 2.0 | 2.1 | 2.1 | 3.7 | 0.1 | 0.1 | 0.3 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 1.1 | 2.1 | 3.2 | 3.5 | 0.3 | -- | -- |
| 957 | 1.9 | 4.1 | 2.3 | 0.9 | 0.7 | 0.0 | 0.4 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 1.0 | 1.6 | 2.8 | 3.4 | 0.3 | 0.4 | 0.4 |
| 960 | 3.1 | 3.0 | 3.0 | 3.0 | 0.7 | 0.5 | 0.1 |
| MEAN | 1.8 | 2.3 | 2.8 | 2.8 | 0.4 | 0.3 | 0.4 |
| SD | 0.68 | 0.87 | 1.98 | 1.32 | 0.35 | 0.24 | 0.19 |
| N | 10 | 10 | 10 | 9 | 10 | 9 | 9 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Eosinophils

STUDY IO: 098
ABBR: Eosinophil

SEX: FEMALE
UNITS: 10³/cmm

| ANIMAL IO | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 0.0 | 0.1 | 0.1 | 0.1 | 0.0 | 0.0 | 0.1 |
| 824 | 0.1 | 0.1 | 0.0 | -- | 0.1 | 0.2 | 0.0 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.2 | 0.1 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 0.0 | 0.1 | 0.1 | 0.1 | 0.2 | 0.2 | 0.1 |
| 831 | 0.4 | 0.0 | 0.2 | 0.0 | 0.0 | 0.1 | 0.1 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 0.0 | 0.3 | 0.1 | 0.0 | 0.0 | 0.0 | 0.0 |
| 835 | 0.1 | 0.1 | 0.0 | 0.0 | 0.1 | 0.1 | 0.0 |
| 836 | 0.2 | 0.2 | 0.2 | 0.1 | 0.0 | 0.0 | 0.1 |
| 837 | 0.3 | 0.1 | 0.0 | 0.0 | 0.1 | 0.2 | 0.1 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 0.0 | 0.1 | 0.2 | 0.2 | 0.4 | 0.1 | 0.0 |
| MEAN | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| SD | 0.14 | 0.09 | 0.09 | 0.07 | 0.13 | 0.09 | 0.05 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 861 | 0.0 | 0.0 | 0.3 | 0.0 | 0.1 | 0.2 | 0.1 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 0.2 | 0.0 | 0.0 | 0.0 | 0.1 | 0.1 | 0.2 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 0.2 | 0.0 | 0.0 | 0.2 | 0.2 | 0.5 | 0.0 |
| 868 | 0.0 | 0.4 | 0.0 | 0.0 | -- | 0.0 | 0.3 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 0.0 | 0.0 | 0.4 | 0.0 | 0.2 | 0.0 | 0.0 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.1 | 0.0 |
| 874 | 0.0 | 0.0 | 0.1 | 0.2 | 0.2 | 0.0 | 0.1 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 0.3 | 0.0 | 0.3 | 0.1 | 0.1 | 0.0 | 0.0 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 0.0 | 0.6 | 0.5 | 0.5 | 0.1 | 0.2 | 0.1 |
| 880 | 0.0 | 0.5 | 0.0 | 0.1 | 0.1 | 0.0 | 0.1 |
| MEAN | 0.1 | 0.2 | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 |
| SD | 0.12 | 0.25 | 0.20 | 0.16 | 0.05 | 0.16 | 0.10 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Eosinophils

STUDY ID: 098
ABBR: Eosinophil

SEX: FEMALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 6.0:6.0 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 901 | 0.3 | 0.3 | 0.3 | 0.3 | 0.0 | 0.1 | 0.1 |
| 902 | 0.0 | 0.1 | 0.2 | 0.3 | 0.2 | 0.1 | 0.2 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 0.4 | 0.0 | 0.0 | 0.0 | -- | 0.1 | 0.1 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 0.0 | 0.1 | 0.1 | 0.3 | 0.0 | 0.0 | 0.0 |
| 909 | 0.1 | 0.1 | 0.2 | 0.1 | 0.1 | 0.2 | 0.0 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 0.2 | 0.0 | 0.2 | -- | 0.1 | 0.3 | 0.3 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 0.2 | 0.2 | 0.0 | 0.4 | 0.1 | 0.1 | 0.2 |
| 916 | 0.2 | 0.1 | 0.0 | 0.1 | 0.1 | 0.0 | 0.2 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 0.0 | 0.5 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 |
| 919 | 0.2 | 0.2 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 |
| 920 | -- | -- | -- | -- | -- | -- | -- |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.2 | 0.2 | 0.1 | 0.2 | 0.1 | 0.1 | 0.1 |
| SD | 0.13 | 0.15 | 0.11 | 0.16 | 0.07 | 0.10 | 0.11 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

GROUP: 18.0:18.0 mg base/kg/day

| | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|
| 941 | 0.0 | 0.2 | 0.0 | 0.1 | 0.3 | 0.1 | 0.2 |
| 942 | 0.0 | 0.0 | 0.1 | -- | 0.0 | 0.6 | 0.0 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 0.2 | 0.0 | 0.2 | 0.0 | 0.3 | 0.2 | 0.2 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 0.3 | 0.0 | 0.0 | 0.0 | 0.4 | 0.3 | 0.0 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 | 0.0 |
| 954 | 0.0 | 0.2 | 0.2 | 0.0 | 0.0 | 0.2 | 0.3 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 0.4 | 0.2 | 0.2 | 0.0 | 0.0 | -- | -- |
| 957 | 0.0 | 0.8 | 0.0 | 0.0 | 0.0 | 0.1 | 0.0 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 0.0 | 0.2 | 0.0 | 0.2 | 0.0 | 0.1 | 0.3 |
| 960 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 | 0.0 |

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| MEAN | 0.1 | 0.2 | 0.1 | 0.0 | 0.1 | 0.2 | 0.1 |
| SD | 0.16 | 0.25 | 0.09 | 0.07 | 0.16 | 0.17 | 0.14 |
| N | 10 | 10 | 10 | 9 | 10 | 9 | 9 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Basophils

STUDY ID: 098
ABBR: Basophils

SEX: FEMALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-----------|--------|--------|--------|---------|---------|---------|---------|
|-----------|--------|--------|--------|---------|---------|---------|---------|

GROUP: 0:0 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 821 | -- | -- | -- | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- | -- | -- | -- |
| 823 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 824 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 825 | -- | -- | -- | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- | -- | -- | -- |
| 827 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 828 | -- | -- | -- | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- | -- | -- | -- |
| 830 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 831 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 832 | -- | -- | -- | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- | -- | -- | -- |
| 834 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 835 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 836 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 837 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.2 |
| 838 | -- | -- | -- | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- | -- | -- | -- |
| 840 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.06 |
| N | 10 | 10 | 10 | 9 | 10 | 10 | 10 |

GROUP: 0.5:0.5 mg base/kg/day

| | | | | | | | |
|------|------|------|------|------|------|------|------|
| 861 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 862 | -- | -- | -- | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- | -- | -- | -- |
| 864 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 865 | -- | -- | -- | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- | -- | -- | -- |
| 867 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 868 | 0.0 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 |
| 869 | -- | -- | -- | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- | -- | -- | -- |
| 871 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 872 | -- | -- | -- | -- | -- | -- | -- |
| 873 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 874 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 875 | -- | -- | -- | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- | -- | -- | -- |
| 877 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 878 | -- | -- | -- | -- | -- | -- | -- |
| 879 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 880 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 10 | 9 | 10 | 10 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL HEMATOLOGY REPORT BY GROUP
TEST: Basophils

STUDY ID: 098
ABBR: Basophils

SEX: FEMALE
UNITS: 10³/cmm

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 | Week 16 | Week 21 | Week 27 |
|-------------------------------|--------|--------|--------|---------|---------|---------|---------|
| GROUP: 6.0:6.0 mg base/kg/day | | | | | | | |
| 901 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 902 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 903 | -- | -- | -- | -- | -- | -- | -- |
| 904 | 0.0 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 |
| 905 | -- | -- | -- | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- | -- | -- | -- |
| 908 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 909 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 910 | -- | -- | -- | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- | -- | -- | -- |
| 912 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 913 | -- | -- | -- | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- | -- | -- | -- |
| 915 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 916 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 917 | -- | -- | -- | -- | -- | -- | -- |
| 918 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 919 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 920 | -- | -- | -- | -- | -- | -- | -- |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 9 | 10 | 10 |

| | | | | | | | |
|---------------------------------|------|------|------|------|------|------|------|
| GROUP: 18.0:18.0 mg base/kg/day | | | | | | | |
| 941 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 942 | 0.0 | 0.0 | 0.0 | -- | 0.0 | 0.0 | 0.0 |
| 943 | -- | -- | -- | -- | -- | -- | -- |
| 944 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 945 | -- | -- | -- | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- | -- | -- | -- |
| 949 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 950 | -- | -- | -- | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- | -- | -- | -- |
| 953 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 954 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 955 | -- | -- | -- | -- | -- | -- | -- |
| 956 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | -- | -- |
| 957 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 958 | -- | -- | -- | -- | -- | -- | -- |
| 959 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 960 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| MEAN | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| SD | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| N | 10 | 10 | 10 | 9 | 10 | 9 | 9 |

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: MALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|--|---|---|---|
| 801 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight |
| 802 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 803 | -- | -- | -- | -- |
| 804 | -- | -- | -- | -- |
| 805 | -- | -- | -- | -- |
| 806 | Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 807 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight |
| 808 | -- | -- | -- | -- |
| 809 | Polychromasia,Slight Macrocytes,Moderate | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 810 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Target Cells, Moderate | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate |
| 811 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Anisocytosis,Slight | Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 812 | -- | -- | -- | Polychromasia,Slight Anisocytosis,Slight |
| 813 | -- | -- | -- | -- |
| 814 | Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 815 | Polychromasia, Moderate; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 0 : 0 mg base/kg/day

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|---|---|---------------------|---|
| 816 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Target Cells,Slight | Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight |
| 817 | -- | -- | -- | -- |
| 818 | -- | -- | -- | -- |
| 819 | -- | -- | -- | -- |
| 820 | -- | -- | -- | -- |

(--) - Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 0 : 0 mg base/kg/day

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|---|--|---|
| 801 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight |
| 802 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 803 | -- | -- | -- |
| 804 | -- | -- | -- |
| 805 | -- | -- | -- |
| 806 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Target Cells,Slight; Anisocytosis,Slight |
| 807 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 808 | -- | -- | -- |
| 809 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 810 | Anisocytosis,Slight; Target Cells,Slight | Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 811 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 812 | -- | -- | -- |
| 813 | -- | -- | -- |
| 814 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: MALE

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|---|---|---|
| 815 | Anisocytosis,Slight; Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 816 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 817 | -- | -- | -- |
| 818 | -- | -- | -- |
| 819 | -- | -- | -- |
| 820 | -- | -- | -- |

(--) -Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 0.5 : 0.5 mg base/kg/day

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|---|--|--|--|
| 841 | -- | -- | -- | -- |
| 842 | -- | -- | -- | -- |
| 843 | -- | -- | -- | -- |
| 844 | Macrocytes, Moderate; Polychromasia, Moderate | Polychromasia, Slight Anisocytosis, Slight | Anisocytosis, Slight | Polychromasia, Slight Target Cells, Slight |
| 845 | -- | -- | -- | -- |
| 846 | Polychromasia, Slight | Polychromasia, Slight Anisocytosis, Slight | Polychromasia, Slight Poikilocytes, Slight; Anisocytosis, Slight | Polychromasia, Slight |
| 847 | -- | -- | -- | -- |
| 848 | Normal Red Blood Cells | Polychromasia, Slight Anisocytosis, Slight | Polychromasia, Slight Anisocytosis, Slight | Polychromasia, Slight Anisocytosis, Slight |
| 849 | -- | -- | -- | -- |
| 850 | Polychromasia, Slight Macrocytes, Slight | Polychromasia, Slight Anisocytosis, Slight | Polychromasia, Slight Anisocytosis, Slight | Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight |
| 851 | Polychromasia, Slight Anisocytosis, Slight | Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight | Polychromasia, Slight Anisocytosis, Slight | Polychromasia, Slight Anisocytosis, Slight |
| 852 | Polychromasia, Moderate; Macrocytes, Slight | Polychromasia, Slight Anisocytosis, Slight; Howell-Jolly Bodies, Slight | Polychromasia, Slight Anisocytosis, Slight | Polychromasia, Slight Target Cells, Slight; Anisocytosis, Slight |
| 853 | Polychromasia, Slight | Anisocytosis, Slight | Target Cells, Slight | Poikilocytes, Slight; Anisocytosis, Slight |
| 854 | -- | -- | -- | -- |
| 855 | -- | -- | -- | -- |
| 856 | -- | -- | -- | -- |
| 857 | -- | -- | -- | -- |
| 858 | Polychromasia, Slight Anisocytosis, Slight | Polychromasia, Slight Anisocytosis, Slight | Anisocytosis, Slight | Polychromasia, Slight Anisocytosis, Slight |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 0.5 : 0.5 mg base/kg/day

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|--|---|---|---|
| 859 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 860 | Polychromasia, Moderate;Macrocytes, Moderate | Polychromasia,Slight Target Cells,Slight; Rouleaux Formation, Slight | Target Cells,Slight; Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 0.5 : 0.5 mg base/kg/day

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|---|--|--|
| 841 | -- | -- | -- |
| 842 | -- | -- | -- |
| 843 | -- | -- | -- |
| 844 | Anisocytosis,Slight; Polychromasia,Slight | Normal Red Blood Cells | Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight |
| 845 | -- | -- | -- |
| 846 | Anisocytosis,Slight; Target Cells,Slight | Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 847 | -- | -- | -- |
| 848 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 849 | -- | -- | -- |
| 850 | Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 851 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight |
| 852 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 853 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight |
| 854 | -- | -- | -- |
| 855 | -- | -- | -- |
| 856 | -- | -- | -- |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 0.5 : 0.5 mg base/kg/day

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|--|---|--|
| 857 | -- | -- | -- |
| 858 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 859 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 860 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight |

(--) - Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: MALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|---|--|--|--|
| 881 | -- | -- | -- | -- |
| 882 | -- | -- | -- | -- |
| 883 | -- | -- | -- | -- |
| 884 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Anisocytosis,Slight | Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 885 | -- | -- | -- | -- |
| 886 | -- | -- | -- | -- |
| 887 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate | -- |
| 888 | -- | -- | -- | -- |
| 889 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 890 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Anisocytosis,Slight |
| 891 | -- | -- | -- | -- |
| 892 | -- | -- | -- | -- |
| 893 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight |
| 894 | -- | -- | -- | -- |
| 895 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 6.0 : 6.0 mg base/kg/day

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|---|--|--|--|
| 896 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 897 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells, Moderate; Anisocytosis, Moderate |
| 898 | -- | -- | -- | -- |
| 899 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Moderate | Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 900 | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 6.0 : 6.0 mg base/kg/day

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|---|---|---|
| 881 | -- | -- | -- |
| 882 | -- | -- | -- |
| 883 | -- | -- | -- |
| 884 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 885 | -- | -- | -- |
| 886 | -- | -- | -- |
| 887 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 888 | -- | -- | -- |
| 889 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 890 | Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 891 | -- | -- | -- |
| 892 | -- | -- | -- |
| 893 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 894 | -- | -- | -- |
| 895 | Anisocytosis,Slight; Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 896 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Normal Red Blood Cells |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: MALE

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|---|--|---|
| 897 | Anisocytosis,Slight; Target Cells,Slight | Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 898 | -- | -- | -- |
| 899 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 900 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |

(--)Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: MALE

GROUP: 18.0 : 18.0 mg base/kg/day

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|--|--|---|--|
| 921 | -- | -- | -- | -- |
| 922 | -- | -- | -- | Polychromasia,Slight Anisocytosis,Slight |
| 923 | Polychromasia, Moderate;Target Cells,Slight; Macrocytes,Moderate | Polychromasia, Moderate; Poikilocytes,Slight; Target Cells, Moderate; Anisocytosis, Moderate | Polychromasia, Moderate; Poikilocytes,Slight; Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight |
| 924 | -- | -- | -- | -- |
| 925 | -- | -- | -- | -- |
| 926 | -- | -- | -- | -- |
| 927 | Polychromasia,Slight Macrocytes,Moderate | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 928 | -- | -- | -- | -- |
| 929 | Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate | Polychromasia,Slight Anisocytosis,Slight |
| 930 | Polychromasia, Moderate; Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate |
| 931 | -- | -- | -- | -- |
| 932 | -- | Polychromasia, Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: MALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|--|--|---|--|
| 933 | Polychromasia,Slight Anisocytosis,Slight; Large Platelets; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis, Moderate | Target Cells, Moderate; Anisocytosis,Slight |
| 934 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | -- |
| 935 | Polychromasia, Moderate;Target Cells,Slight; Macrocytes,Moderate; Howell-Jolly Bodies, Moderate | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate |
| 936 | -- | -- | -- | -- |
| 937 | Polychromasia,Slight Target Cells,Slight; Macrocytes,Slight | -- | -- | -- |
| 938 | -- | -- | -- | -- |
| 939 | Polychromasia,Slight Target Cells,Slight; Macrocytes,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight | Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight |
| 940 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia, Moderate; Poikilocytes,Slight; Target Cells,Slight; Anisocytosis, Moderate | Polychromasia, Moderate; Poikilocytes,Slight; Target Cells, Moderate; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Moderate |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 093

SEX: MALE

GROUP: 18.0 : 18.0 mg base/kg/day

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|--|---|---|
| 921 | -- | -- | -- |
| 922 | Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight |
| 923 | Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 924 | -- | -- | -- |
| 925 | -- | -- | -- |
| 926 | -- | -- | -- |
| 927 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 928 | -- | -- | -- |
| 929 | Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 930 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 931 | -- | -- | -- |
| 932 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 933 | Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 934 | -- | -- | -- |
| 935 | Anisocytosis,Slight; Target Cells,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 093

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: MALE

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|--|---|--|
| 936 | -- | -- | -- |
| 937 | -- | -- | -- |
| 938 | -- | -- | -- |
| 939 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 940 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia;Slight | Target Cells,Slight; Anisocytosis,Slight |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|---|--|---|---|
| 821 | -- | -- | -- | -- |
| 822 | -- | -- | -- | -- |
| 823 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Anisocytosis,Slight | Target Cells,Slight; Anisocytosis,Slight |
| 824 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | -- |
| 825 | -- | -- | -- | -- |
| 826 | -- | -- | -- | -- |
| 827 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 828 | -- | -- | -- | -- |
| 829 | -- | -- | -- | -- |
| 830 | Polychromasia,Slight Macrocytes,Moderate | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 831 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 832 | -- | -- | -- | -- |
| 833 | -- | -- | -- | -- |
| 834 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 835 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate |
| 836 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|---|---|---|---|
| 837 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 838 | -- | -- | -- | -- |
| 839 | -- | -- | -- | -- |
| 840 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0 : 0 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|---|---|--|
| 821 | -- | -- | -- |
| 822 | -- | -- | -- |
| 823 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 824 | Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate |
| 825 | -- | -- | -- |
| 826 | -- | -- | -- |
| 827 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis, Moderate;Crenation, Slight |
| 828 | -- | -- | -- |
| 829 | -- | -- | -- |
| 830 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 831 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 832 | -- | -- | -- |
| 833 | -- | -- | -- |
| 834 | Anisocytosis,Slight; Polychromasia,Slight | Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 835 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: FEMALE

GROUP: 0 : 0 mg base/kg/day

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|---|--|--|
| 836 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 837 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 838 | -- | -- | -- |
| 839 | -- | -- | -- |
| 840 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |

(---)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0.5 : 0.5 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|--|--|---|---|
| 861 | Polychromasia,Slight Macrocytes,Moderate | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 862 | -- | -- | -- | -- |
| 863 | -- | -- | -- | -- |
| 864 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 865 | -- | -- | -- | -- |
| 866 | -- | -- | -- | -- |
| 867 | Target Cells,Slight; Macrocytes,Moderate; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 868 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 869 | -- | -- | -- | -- |
| 870 | -- | -- | -- | -- |
| 871 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 872 | -- | -- | -- | -- |
| 873 | Polychromasia,Slight Poikilocytes,Slight; Macrocytes,Moderate | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight | Target Cells,Slight |
| 874 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight |
| 875 | -- | -- | -- | -- |
| 876 | -- | -- | -- | -- |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0.5 : 0.5 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|--|---|---|--|
| 877 | Polychromasia, Moderate;Macrocytes, Moderate | Polychromasia,Slight Anisocytosis,Slight | Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 878 | -- | -- | -- | -- |
| 879 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 880 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 093

GROUP: 0.5 : 0.5 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|---|---|---|
| 861 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight |
| 862 | -- | -- | -- |
| 863 | -- | -- | -- |
| 864 | Anisocytosis,Slight; Target Cells,Slight | Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 865 | -- | -- | -- |
| 866 | -- | -- | -- |
| 867 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 868 | -- | Polychromasia,Slight | Anisocytosis,Slight |
| 869 | -- | -- | -- |
| 870 | -- | -- | -- |
| 871 | Anisocytosis, Moderate; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 872 | -- | -- | -- |
| 873 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 874 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 875 | -- | -- | -- |
| 876 | -- | -- | -- |
| 877 | Anisocytosis,Slight; Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 878 | -- | -- | -- |
| 879 | Anisocytosis,Slight; Polychromasia,Slight | Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 0.5 : 0.5 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|--|---|---|
| 880 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|---|---|---|--|
| 901 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 902 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Anisocytosis, Moderate | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 903 | -- | -- | -- | -- |
| 904 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight |
| 905 | -- | -- | -- | -- |
| 906 | -- | -- | -- | -- |
| 907 | -- | -- | -- | -- |
| 908 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate |
| 909 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 910 | -- | -- | -- | -- |
| 911 | -- | -- | -- | -- |
| 912 | Polychromasia,Slight Target Cells,Slight; Macrocytes,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate | -- |
| 913 | -- | -- | -- | -- |
| 914 | -- | -- | -- | -- |
| 915 | Polychromasia,Slight Anisocytosis | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate | Polychromasia,Slight Anisocytosis, Moderate | Polychromasia,Slight Anisocytosis,Slight |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 6.0 : 6.0 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|--|---|---|--|
| 916 | Polychromasia, Moderate;Macrocytes, Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Target Cells,Slight; Anisocytosis,Slight |
| 917 | -- | -- | -- | -- |
| 918 | Polychromasia,Slight Macrocytes,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight |
| 919 | Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 920 | -- | -- | -- | -- |

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: FEMALE

GROUP: 6.0 : 6.0 mg base/kg/day

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|--|---|---|
| 901 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 902 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 903 | -- | -- | -- |
| 904 | -- | Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 905 | -- | -- | -- |
| 906 | -- | -- | -- |
| 907 | -- | -- | -- |
| 908 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 909 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 910 | -- | -- | -- |
| 911 | -- | -- | -- |
| 912 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 913 | -- | -- | -- |
| 914 | -- | -- | -- |
| 915 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 916 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 917 | -- | -- | -- |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

SEX: FEMALE

GROUP: 6.0 : 6.0 mg base/kg/day

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|--|---|---|
| 918 | Anisocytosis,Slight; Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 919 | Anisocytosis,Slight; Polychromasia,Slight | Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 920 | -- | -- | -- |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 093

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|--|--|---|--|
| 941 | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Poikilocytes,Slight; Anisocytosis, Moderate | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis, Moderate |
| 942 | Polychromasia, Moderate;Macrocytes, Moderate | Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate | Clotted Sample |
| 943 | -- | -- | -- | -- |
| 944 | Anisocytosis, Moderate; Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 945 | -- | -- | -- | -- |
| 946 | -- | -- | -- | -- |
| 947 | -- | -- | -- | -- |
| 948 | -- | -- | -- | -- |
| 949 | Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight | Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate |
| 950 | -- | -- | -- | -- |
| 951 | -- | -- | -- | -- |
| 952 | -- | -- | -- | -- |
| 953 | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 2 | Week 4 | Week 8 | Week 13 |
|-----------|--|--|--|--|
| 954 | Polychromasia, Moderate;Target Cells,Slight; Macrocytes,Moderate; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight | Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight |
| 955 | -- | -- | -- | -- |
| 956 | Polychromasia, Moderate;Macrocytes, Moderate | Polychromasia,Slight Anisocytosis, Moderate; Howell-Jolly Bodies, Slight | Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight |
| 957 | Polychromasia,Slight Poikilocytes, Moderate;Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Mod. to Marked;Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 958 | -- | -- | -- | -- |
| 959 | Polychromasia, Moderate;Macrocytes, Moderate | Polychromasia,Slight Target Cells,Slight; Anisocytosis, Moderate; Howell-Jolly Bodies, Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis, Moderate | Polychromasia, Moderate;Target Cells,Moderate; Anisocytosis, Moderate |
| 960 | Polychromasia,Slight Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Moderate | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia, Moderate;Target Cells,Slight; Anisocytosis,Mod. to Marked |

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

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MORPHOLOGY OBSERVATIONS

STUDY ID: 098

GROUP: 18.0 : 18.0 mg base/kg/day

SEX: FEMALE

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|--|---|---|
| 941 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells, Moderate; Anisocytosis,Slight |
| 942 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 943 | -- | -- | -- |
| 944 | Anisocytosis,Slight; Polychromasia,Slight Howell-Jolly Bodies, Slight | Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 945 | -- | -- | -- |
| 946 | -- | -- | -- |
| 947 | -- | -- | -- |
| 948 | -- | -- | -- |
| 949 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 950 | -- | -- | -- |
| 951 | -- | -- | -- |
| 952 | -- | -- | -- |
| 953 | Anisocytosis,Slight; Polychromasia, Moderate;Target Cells,Slight; Howell-Jolly Bodies, Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 954 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Target Cells,Slight; Anisocytosis,Slight |
| 955 | -- | -- | -- |
| 956 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | -- | -- |

(--)-Data Unavailable

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 078

SEX: FEMALE

GROUP: 18.0 : 18.0 mg base/kg/day

| ANIMAL ID | Week 16 | Week 21 | Week 27 |
|-----------|---|---|--|
| 957 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight; Howell-Jolly Bodies, Slight |
| 958 | -- | -- | -- |
| 959 | Anisocytosis, Moderate; Polychromasia,Slight Target Cells,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight | Polychromasia,Slight Anisocytosis,Slight |
| 960 | Anisocytosis,Slight; Polychromasia,Slight | Polychromasia,Slight Anisocytosis,Slight | Polychromasia,Slight Target Cells,Slight; Anisocytosis,Slight; Howell-Jolly Bodies, Slight |

(--)-Data Unavailable

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APPENDIX 8
Ophthalmology Report

ANIMAL EYE ASSOCIATES

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DRAFT

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OPHTHALMIC REPORT

UIC/TRL Study No. 098


THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

On December 9, 1992, (Week -1), a sufficient number of Sprague Dawley rats were given ophthalmic examinations by indirect ophthalmoscopy to result in eighty males and eighty females suitable for the study.

On March 10, 1993 (Week 12), I re-examined the remaining 155 rats. One mid dose male was diagnosed with corneal neovascularization and a cataract, and one low dose female demonstrated a cataract. In both cases, the fundus was not visible. Both lesions were of traumatic origin and were not treatment-related. In addition, ocular lesions were not seen in high dose animals. All other rats appeared similar (no lesions) to the previous pretest examinations done on December 9, 1992.

On June 9, 1993 (Week 26), I re-examined the remaining 79 rats. All observed lesions were considered incidental as they were not seen in Week 12 and a dose-related pattern was not apparent. At this time, one low dose male was diagnosed with corneal keratitis and corneal neovascularization; a second low dose male demonstrated a cortical opacity of the lens. Retinal degeneration and optic nerve degeneration were diagnosed in one mid dose male and a cataract (fundus not visible) was seen in a mid dose male and a mid dose female. In two low dose females, corneal neovascularization and lens endophthalmitis were seen, with one of these two diagnosed rats also displaying a cataract. The fundus was not visible in either rat. One high dose female was diagnosed with retinal degeneration, optic nerve degeneration and a mild cataract. In all cases, lesions were of traumatic origin and were not treatment-related. All remaining rats appeared similar (no lesions) to previous examinations.

Sincerely,


Samuel J. Vainisi, D.V.M.
Professor of Comparative
Ophthalmology - U. of IL. at Chicago

Diplomate, American College of
Veterinary Ophthalmologists

7/21/93

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

Ophthalmic Examinations
Males

| Dose (mg/kg/day) | Animal Number | Week -1 | | Week 12 | | Week 26 | |
|---------------------|------------------|---------|------|---------|------|---------|------|
| | | R.E. | L.E. | R.E. | L.E. | R.E. | L.E. |
| 0 | 801 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 802 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 803 | WNL | WNL | WNL | WNL | - | - |
| | 804 | WNL | WNL | WNL | WNL | - | - |
| | 805 | WNL | WNL | WNL | WNL | - | - |
| | 806 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 807 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 808 | WNL | WNL | WNL | WNL | - | - |
| | 809 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 810 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 811 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 812 | WNL | WNL | WNL | WNL | - | - |
| | 813 | WNL | WNL | WNL | WNL | - | - |
| | 814 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 815 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 816 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 817 | WNL | WNL | WNL | WNL | - | - |
| | 818 | WNL | WNL | WNL | WNL | - | - |
| | 819 | WNL | WNL | WNL | WNL | - | - |
| | 820 | WNL | WNL | WNL | WNL | - | - |
| 0.5 | 841 | WNL | WNL | WNL | WNL | - | - |
| | 842 | WNL | WNL | WNL | WNL | - | - |
| | 843 | WNL | WNL | WNL | WNL | - | - |
| | 844 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 845 | WNL | WNL | WNL | WNL | - | - |
| | 846 | WNL | WNL | WNL | WNL | CKT/CN | WNL |
| | 847 | WNL | WNL | WNL | WNL | - | - |
| | 848 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 849 | WNL | WNL | WNL | WNL | - | - |
| | 850 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 851 | WNL | WNL | WNL | WNL | WNL | COL |
| | 852 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 853 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 854 | WNL | WNL | WNL | WNL | - | - |
| | 855 | WNL | WNL | WNL | WNL | - | - |
| | 856 | WNL | WNL | WNL | WNL | - | - |
| | 857 | WNL | WNL | WNL | WNL | - | - |
| | 858 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 859 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 860 | WNL | WNL | WNL | WNL | WNL | WNL |

Dose = mg base/kg/day
 R.E. = Right Eye
 L.E. = Left Eye
 * = Animal Previously Died
 - = Animal Previously Sacrificed
 WNL = Within Normal Limits
 CKT = Corneal Keratitis
 CN = Corneal Neovascularization
 LC = Lens Cataract
 LE = Lens Endophthalmitis
 FNV = Fundus Not Visible
 MC = Mild Cataract
 COL = Cortical Opacity of Lens
 RD = Retinal Degeneration
 OND = Optic Nerve Degeneration (Gliosis)

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238609
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

Ophthalmic Examinations
Males

| Dose (mg/kg/day) | Animal Number | Week -1 | | Week 12 | | Week 26 | |
|---------------------|------------------|---------|------|-----------|------|---------|------|
| | | R.E. | L.E. | R.E. | L.E. | R.E. | L.E. |
| 6 | 881 | WNL | WNL | WNL | WNL | - | - |
| | 882 | WNL | WNL | WNL | WNL | - | - |
| | 883 | WNL | WNL | WNL | WNL | - | - |
| | 884 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 885 | WNL | WNL | WNL | WNL | - | - |
| | 886 | WNL | WNL | WNL | WNL | - | - |
| | 887 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 888 | WNL | WNL | WNL | WNL | * | * |
| | 889 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 890 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 891 | WNL | WNL | WNL | WNL | - | - |
| | 892 | WNL | WNL | WNL | WNL | - | - |
| | 893 | WNL | WNL | WNL | WNL | RD/OND | WNL |
| | 894 | WNL | WNL | WNL | WNL | - | - |
| | 895 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 896 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 897 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 898 | WNL | WNL | WNL | WNL | - | - |
| | 899 | WNL | WNL | LC/CN/FNV | WNL | LC/FNV | WNL |
| | 900 | WNL | WNL | WNL | WNL | WNL | WNL |
| 18 | 921 | WNL | WNL | * | * | * | * |
| | 922 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 923 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 924 | WNL | WNL | WNL | WNL | - | - |
| | 925 | WNL | WNL | WNL | WNL | - | - |
| | 926 | WNL | WNL | * | * | * | * |
| | 927 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 928 | WNL | WNL | WNL | WNL | - | - |
| | 929 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 930 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 931 | WNL | WNL | WNL | WNL | - | - |
| | 932 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 933 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 934 | WNL | WNL | * | * | * | * |
| | 935 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 936 | WNL | WNL | * | * | * | * |
| | 937 | WNL | WNL | * | * | * | * |
| | 938 | WNL | WNL | WNL | WNL | - | - |
| | 939 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 940 | WNL | WNL | WNL | WNL | WNL | WNL |

Dose = mg base/kg/day
 R.E. = Right Eye
 L.E. = Left Eye
 * = Animal Previously Died
 - = Animal Previously Sacrificed
 WNL = Within Normal Limits
 CKT = Corneal Keratitis
 CN = Corneal Neovascularization
 LC = Lens Cataract
 LE = Lens Endophthalmitis
 FNV = Fundus Not Visible
 MC = Mild Cataract
 COL = Cortical Opacity of Lens
 RD = Retinal Degeneration
 OND = Optic Nerve Degeneration (Gliosis)

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

Ophthalmic Examinations
Females

DRAFT

| Dose (mg/kg/day) | Animal Number | Week -1 | | Week 12 | | Week 26 | |
|---------------------|------------------|---------|------|---------|------|------------|------|
| | | R.E. | L.E. | R.E. | L.E. | R.E. | L.E. |
| 0 | 821 | WNL | WNL | WNL | WNL | - | - |
| | 822 | WNL | WNL | WNL | WNL | - | - |
| | 823 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 824 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 825 | WNL | WNL | WNL | WNL | - | - |
| | 826 | WNL | WNL | WNL | WNL | - | - |
| | 827 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 828 | WNL | WNL | WNL | WNL | - | - |
| | 829 | WNL | WNL | WNL | WNL | - | - |
| | 830 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 831 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 832 | WNL | WNL | WNL | WNL | - | - |
| | 833 | WNL | WNL | WNL | WNL | - | - |
| | 834 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 835 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 836 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 837 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 838 | WNL | WNL | WNL | WNL | - | - |
| | 839 | WNL | WNL | WNL | WNL | - | - |
| | 840 | WNL | WNL | WNL | WNL | WNL | WNL |
| 0.5 | 861 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 862 | WNL | WNL | WNL | WNL | - | - |
| | 863 | WNL | WNL | WNL | WNL | - | - |
| | 864 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 865 | WNL | WNL | WNL | WNL | - | - |
| | 866 | WNL | WNL | WNL | WNL | - | - |
| | 867 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 868 | WNL | WNL | WNL | WNL | LCN/LE/FNV | WNL |
| | 869 | WNL | WNL | WNL | WNL | - | - |
| | 870 | WNL | WNL | WNL | WNL | - | - |
| | 871 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 872 | WNL | WNL | WNL | WNL | - | - |
| | 873 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 874 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 875 | WNL | WNL | WNL | WNL | - | - |
| | 876 | WNL | WNL | WNL | WNL | - | - |
| | 877 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 878 | WNL | WNL | WNL | WNL | - | - |
| | 879 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 880 | WNL | WNL | LC/FNV | WNL | CN/LE/FNV | WNL |

Dose = mg base/kg/day
 R.E. = Right Eye
 L.E. = Left Eye
 * = Animal Previously Died
 - = Animal Previously Sacrificed
 WNL = Within Normal Limits
 CKT = Corneal Keratitis
 CN = Corneal Neovascularization
 LC = Lens Cataract
 LE = Lens Endophthalmitis
 FNV = Fundus Not Visible
 MC = Mild Cataract
 COL = Cortical Opacity of Lens
 RD = Retinal Degeneration
 OND = Optic Nerve Degeneration (Gliosis)

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

Ophthalmic Examinations
Females

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| Dose (mg/kg/day) | Animal Number | Week -1 | | Week 12 | | Week 26 | |
|---------------------|------------------|---------|------|---------|------|-----------|------|
| | | R.E. | L.E. | R.E. | L.E. | R.E. | L.E. |
| 6 | 901 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 902 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 903 | WNL | WNL | WNL | WNL | - | - |
| | 904 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 905 | WNL | WNL | WNL | WNL | - | - |
| | 906 | WNL | WNL | WNL | WNL | - | - |
| | 907 | WNL | WNL | WNL | WNL | - | - |
| | 908 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 909 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 910 | WNL | WNL | WNL | WNL | - | - |
| | 911 | WNL | WNL | WNL | WNL | - | - |
| | 912 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 913 | WNL | WNL | WNL | WNL | - | - |
| | 914 | WNL | WNL | WNL | WNL | - | - |
| | 915 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 916 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 917 | WNL | WNL | WNL | WNL | - | - |
| | 918 | WNL | WNL | WNL | WNL | LC/FNV | WNL |
| | 919 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 920 | WNL | WNL | WNL | WNL | - | - |
| 18 | 941 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 942 | WNL | WNL | WNL | WNL | RD/OND/MC | WNL |
| | 943 | WNL | WNL | WNL | WNL | - | - |
| | 944 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 945 | WNL | WNL | WNL | WNL | - | - |
| | 946 | WNL | WNL | WNL | WNL | - | - |
| | 947 | WNL | WNL | WNL | WNL | - | - |
| | 948 | WNL | WNL | WNL | WNL | - | - |
| | 949 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 950 | WNL | WNL | WNL | WNL | - | - |
| | 951 | WNL | WNL | WNL | WNL | - | - |
| | 952 | WNL | WNL | WNL | WNL | - | - |
| | 953 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 954 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 955 | WNL | WNL | WNL | WNL | - | - |
| | 956 | WNL | WNL | WNL | WNL | * | * |
| | 957 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 958 | WNL | WNL | WNL | WNL | - | - |
| | 959 | WNL | WNL | WNL | WNL | WNL | WNL |
| | 960 | WNL | WNL | WNL | WNL | WNL | WNL |

Dose = mg base/kg/day
 R.E. = Right Eye
 L.E. = Left Eye
 * = Animal Previously Died
 - = Animal Previously Sacrificed
 WNL = Within Normal Limits
 CKT = Corneal Keratitis
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 LC = Lens Cataract
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 FNV = Fundus Not Visible
 MC = Mild Cataract
 COL = Cortical Opacity of Lens
 RD = Retinal Degeneration
 OND = Optic Nerve Degeneration (Gliosis)

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APPENDIX 9

Individual Organ Weights

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 1M - 0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 801 | 802 | 803 | 804 | 805 | 806 | 807 | 808 | 809 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| BODY WEIGHT (G) | 627.6 | 561.7 | 497.7 | 497.6 | 560.5 | 555.8 | 502.4 | 564.8 | 622.4 |
| Adrenals (pr) (G) | 0.050 | 0.050 | 0.083 | 0.061 | 0.079 | 0.080 | 0.070 | 0.075 | 0.090 |
| % BODY WEIGHT | 0.008 | 0.009 | 0.017 | 0.012 | 0.014 | 0.014 | 0.014 | 0.013 | 0.014 |
| Brain (G) | 2.190 | 2.120 | 2.147 | 2.152 | 2.111 | 2.160 | 2.190 | 2.329 | 2.180 |
| % BODY WEIGHT | 0.349 | 0.377 | 0.431 | 0.432 | 0.377 | 0.389 | 0.436 | 0.412 | 0.350 |
| Heart (G) | 1.880 | 1.630 | 1.625 | 1.494 | 1.583 | 1.710 | 1.410 | 1.760 | 2.040 |
| % BODY WEIGHT | 0.300 | 0.290 | 0.327 | 0.300 | 0.282 | 0.308 | 0.281 | 0.312 | 0.328 |
| Kidneys (pr) (G) | 4.400 | 4.270 | 3.723 | 3.670 | 3.731 | 4.550 | 3.470 | 4.085 | 4.420 |
| % BODY WEIGHT | 0.701 | 0.760 | 0.748 | 0.738 | 0.666 | 0.819 | 0.691 | 0.723 | 0.710 |
| Liver (G) | 19.880 | 19.940 | 17.653 | 15.586 | 17.219 | 18.520 | 14.800 | 15.689 | 18.760 |
| % BODY WEIGHT | 3.168 | 3.550 | 3.547 | 3.132 | 3.072 | 3.332 | 2.946 | 2.778 | 3.014 |
| Spleen (G) | 0.750 | 0.730 | 0.632 | 0.737 | 0.771 | 0.780 | 0.680 | 0.793 | 0.940 |
| % BODY WEIGHT | 0.120 | 0.130 | 0.127 | 0.148 | 0.138 | 0.140 | 0.135 | 0.140 | 0.151 |
| Testes w/Epidid. (pr) (G) | 5.700 | 5.370 | 5.282 | 5.045 | 5.463 | 5.110 | 5.260 | 5.505 | 6.110 |
| % BODY WEIGHT | 0.908 | 0.956 | 1.061 | 1.014 | 0.975 | 0.919 | 1.047 | 0.975 | 0.982 |

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 1M - 0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 810 | 811 | 812 | 813 | 814 | 815 | 816 | 817 | 818 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| BODY WEIGHT (G) | 546.4 | 609.8 | 473.6 | 436.0 | 602.0 | 709.8 | 707.9 | 501.2 | 525.8 |
| Adrenals (pr) (G) | 0.070 | 0.090 | 0.059 | 0.055 | 0.080 | 0.090 | 0.090 | 0.059 | 0.055 |
| % BODY WEIGHT | 0.013 | 0.015 | 0.012 | 0.013 | 0.013 | 0.013 | 0.013 | 0.012 | 0.010 |
| Brain (G) | 2.110 | 2.010 | 2.206 | 2.091 | 2.200 | 2.250 | 2.310 | 2.132 | 2.153 |
| % BODY WEIGHT | 0.386 | 0.330 | 0.466 | 0.480 | 0.365 | 0.317 | 0.326 | 0.425 | 0.409 |
| Heart (G) | 1.580 | 1.710 | 1.536 | 1.464 | 1.790 | 2.200 | 2.210 | 1.449 | 1.626 |
| % BODY WEIGHT | 0.289 | 0.280 | 0.324 | 0.336 | 0.297 | 0.310 | 0.312 | 0.289 | 0.309 |
| Kidneys (pr) (G) | 3.780 | 4.780 | 4.221 | 3.443 | 4.020 | 4.880 | 4.980 | 4.002 | 3.916 |
| % BODY WEIGHT | 0.692 | 0.784 | 0.891 | 0.790 | 0.668 | 0.688 | 0.703 | 0.798 | 0.745 |
| Liver (G) | 16.980 | 18.720 | 14.103 | 13.903 | 18.120 | 24.760 | 26.660 | 14.234 | 16.077 |
| % BODY WEIGHT | 3.108 | 3.070 | 2.978 | 3.189 | 3.010 | 3.488 | 3.766 | 2.840 | 3.058 |
| Spleen (G) | 0.800 | 0.970 | 0.784 | 0.667 | 0.740 | 1.020 | 1.070 | 0.788 | 0.921 |
| % BODY WEIGHT | 0.146 | 0.159 | 0.166 | 0.153 | 0.123 | 0.144 | 0.151 | 0.157 | 0.175 |
| Testes w/Epidid. (pr) (G) | 5.800 | 4.940 | 5.718 | 4.408 | 5.290 | 4.970 | 5.790 | 5.143 | 5.129 |
| % BODY WEIGHT | 1.061 | 0.810 | 1.207 | 1.011 | 0.879 | 0.700 | 0.818 | 1.026 | 0.975 |

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALEGROUP: 1M - 0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 819 | 820 |
|----------------------------|--------|--------|
| BODY WEIGHT (G) | 505.0 | 565.9 |
| Adrenals (pr) (G) | 0.071 | 0.061 |
| % BODY WEIGHT | 0.014 | 0.011 |
| Brain (G) | 1.974 | 1.990 |
| % BODY WEIGHT | 0.391 | 0.352 |
| Heart (G) | 1.606 | 1.568 |
| % BODY WEIGHT | 0.318 | 0.277 |
| Kidneys (pr) (G) | 3.939 | 4.057 |
| % BODY WEIGHT | 0.780 | 0.717 |
| Liver (G) | 15.583 | 20.395 |
| % BODY WEIGHT | 3.086 | 3.604 |
| Spleen (G) | 0.939 | 0.819 |
| % BODY WEIGHT | 0.186 | 0.145 |
| Testes w/Epidid. (pr) (G) | 5.624 | 5.248 |
| % BODY WEIGHT | 1.114 | 0.927 |

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 2M - 0.5 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 841 | 842 | 843 | 844 | 845 | 846 | 847 | 848 | 849 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| BODY WEIGHT (G) | 462.8 | 486.3 | 495.1 | 518.4 | 562.1 | 511.5 | 508.3 | 591.2 | 550.7 |
| Adrenals (pr) (G) | 0.052 | 0.059 | 0.054 | 0.060 | 0.067 | 0.090 | 0.071 | 0.070 | 0.062 |
| % BODY WEIGHT | 0.011 | 0.012 | 0.011 | 0.012 | 0.012 | 0.018 | 0.014 | 0.012 | 0.011 |
| Brain (G) | 2.137 | 2.161 | 2.066 | 2.180 | 2.136 | 2.110 | 2.195 | 1.980 | 2.277 |
| % BODY WEIGHT | 0.462 | 0.444 | 0.417 | 0.421 | 0.380 | 0.413 | 0.432 | 0.335 | 0.413 |
| Heart (G) | 1.534 | 1.816 | 1.944 | 1.510 | 1.691 | 1.440 | 1.763 | 1.980 | 1.669 |
| % BODY WEIGHT | 0.331 | 0.373 | 0.393 | 0.291 | 0.301 | 0.282 | 0.347 | 0.335 | 0.303 |
| Kidneys (pr) (G) | 3.900 | 3.878 | 4.266 | 3.610 | 4.059 | 3.450 | 4.002 | 3.920 | 3.911 |
| % BODY WEIGHT | 0.843 | 0.797 | 0.862 | 0.696 | 0.722 | 0.674 | 0.787 | 0.663 | 0.710 |
| Liver (G) | 16.079 | 17.733 | 18.379 | 13.150 | 20.133 | 12.930 | 16.575 | 15.620 | 16.714 |
| % BODY WEIGHT | 3.474 | 3.647 | 3.712 | 2.537 | 3.582 | 2.528 | 3.261 | 2.642 | 3.035 |
| Spleen (G) | 0.934 | 0.891 | 0.699 | 0.880 | 0.836 | 0.700 | 0.822 | 0.740 | 1.032 |
| % BODY WEIGHT | 0.202 | 0.183 | 0.141 | 0.170 | 0.149 | 0.137 | 0.162 | 0.125 | 0.187 |
| Testes w/Epidid. (pr) (G) | 4.945 | 4.996 | 5.311 | 5.400 | 5.583 | 5.220 | 4.888 | 5.260 | 4.609 |
| % BODY WEIGHT | 1.068 | 1.027 | 1.073 | 1.042 | 0.993 | 1.021 | 0.962 | 0.890 | 0.837 |

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 2M - 0.5 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 850 | 851 | 852 | 853 | 854 | 855 | 856 | 857 | 858 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| BODY WEIGHT (G) | 549.0 | 572.9 | 617.4 | 614.0 | 523.9 | 585.5 | 553.0 | 422.2 | 623.5 |
| Adrenals (pr) (G) | 0.040 | 0.080 | 0.070 | 0.050 | 0.058 | 0.070 | 0.044 | 0.054 | 0.080 |
| % BODY WEIGHT | 0.007 | 0.014 | 0.011 | 0.008 | 0.011 | 0.012 | 0.008 | 0.013 | 0.013 |
| Brain (G) | 2.160 | 2.260 | 2.290 | 2.060 | 2.072 | 2.216 | 2.222 | 1.999 | 2.040 |
| % BODY WEIGHT | 0.393 | 0.394 | 0.371 | 0.336 | 0.395 | 0.378 | 0.402 | 0.473 | 0.327 |
| Heart (G) | 1.530 | 1.770 | 1.920 | 1.730 | 1.757 | 1.687 | 1.778 | 1.365 | 1.870 |
| % BODY WEIGHT | 0.279 | 0.309 | 0.311 | 0.282 | 0.335 | 0.288 | 0.322 | 0.323 | 0.300 |
| Kidneys (pr) (G) | 4.020 | 4.850 | 4.300 | 3.800 | 4.142 | 4.216 | 4.429 | 3.896 | 4.560 |
| % BODY WEIGHT | 0.732 | 0.847 | 0.696 | 0.619 | 0.791 | 0.720 | 0.801 | 0.923 | 0.731 |
| Liver (G) | 15.780 | 19.710 | 20.610 | 17.490 | 17.281 | 18.802 | 19.823 | 12.017 | 20.100 |
| % BODY WEIGHT | 2.874 | 3.440 | 3.338 | 2.849 | 3.299 | 3.211 | 3.585 | 2.846 | 3.224 |
| Spleen (G) | 0.730 | 0.850 | 0.950 | 0.810 | 0.994 | 1.050 | 0.923 | 0.634 | 0.950 |
| % BODY WEIGHT | 0.133 | 0.148 | 0.154 | 0.132 | 0.190 | 0.179 | 0.167 | 0.150 | 0.152 |
| Testes w/Epidid. (pr) (G) | 5.020 | 5.560 | 6.010 | 6.030 | 4.894 | 5.630 | 5.985 | 4.501 | 5.640 |
| % BODY WEIGHT | 0.914 | 0.971 | 0.973 | 0.982 | 0.934 | 0.962 | 1.082 | 1.066 | 0.905 |

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 2M - 0.5 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 859 | 860 |
|----------------------------|--------|--------|
| BODY WEIGHT (G) | 653.2 | 649.0 |
| Adrenals (pr) (G) | 0.070 | 0.050 |
| % BODY WEIGHT | 0.011 | 0.008 |
| Brain (G) | 2.170 | 2.260 |
| % BODY WEIGHT | 0.332 | 0.348 |
| Heart (G) | 1.820 | 1.740 |
| % BODY WEIGHT | 0.279 | 0.268 |
| Kidneys (pr) (G) | 4.630 | 5.250 |
| % BODY WEIGHT | 0.709 | 0.809 |
| Liver (G) | 19.210 | 22.530 |
| % BODY WEIGHT | 2.941 | 3.471 |
| Spleen (G) | 0.780 | 1.060 |
| % BODY WEIGHT | 0.119 | 0.163 |
| Testes w/Epidid. (pr) (G) | 5.970 | 5.730 |
| % BODY WEIGHT | 0.914 | 0.883 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 3M - 6.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 881 | 882 | 883 | 884 | 885 | 886 | 887 | 888 | 889 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| BODY WEIGHT (G) | 403.7 | 476.6 | 392.9 | 515.8 | 418.0 | 371.7 | 565.5 | 472.8 | 678.0 |
| Adrenals (pr) (G) | 0.041 | 0.097 | 0.084 | 0.100 | 0.052 | 0.048 | 0.050 | 0.059 | 0.080 |
| % BODY WEIGHT | 0.010 | 0.020 | 0.021 | 0.019 | 0.012 | 0.013 | 0.009 | 0.012 | 0.012 |
| Brain (G) | 2.189 | 2.268 | 2.029 | 1.950 | 2.060 | 2.039 | 1.990 | 2.067 | 2.220 |
| % BODY WEIGHT | 0.542 | 0.476 | 0.516 | 0.378 | 0.493 | 0.549 | 0.352 | 0.437 | 0.327 |
| Heart (G) | 1.211 | 1.960 | 1.542 | 1.540 | 1.785 | 1.373 | 1.620 | 1.707 | 1.940 |
| % BODY WEIGHT | 0.300 | 0.411 | 0.392 | 0.299 | 0.427 | 0.369 | 0.286 | 0.361 | 0.286 |
| Kidneys (pr) (G) | 3.689 | 4.433 | 4.126 | 4.270 | 3.590 | 3.821 | 3.780 | 4.859 | 4.220 |
| % BODY WEIGHT | 0.914 | 0.930 | 1.050 | 0.828 | 0.859 | 1.028 | 0.668 | 1.028 | 0.622 |
| Liver (G) | 12.294 | 17.454 | 15.026 | 16.000 | 17.269 | 13.869 | 16.430 | 21.403 | 20.390 |
| % BODY WEIGHT | 3.045 | 3.662 | 3.824 | 3.102 | 4.131 | 3.731 | 2.905 | 4.527 | 3.007 |
| Spleen (G) | 1.076 | 1.281 | 1.062 | 0.820 | 1.563 | 1.247 | 0.780 | 1.747 | 0.960 |
| % BODY WEIGHT | 0.267 | 0.269 | 0.270 | 0.159 | 0.374 | 0.335 | 0.138 | 0.370 | 0.142 |
| Testes w/Epidid. (pr) (G) | 5.340 | 5.178 | 5.056 | 5.710 | 4.955 | 5.155 | 4.880 | 4.912 | 6.280 |
| % BODY WEIGHT | 1.323 | 1.086 | 1.287 | 1.107 | 1.185 | 1.387 | 0.863 | 1.039 | 0.926 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 3M - 6.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 890 | 891 | 892 | 893 | 894 | 895 | 896 | 897 | 898 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| BODY WEIGHT (G) | 579.4 | 404.7 | 431.8 | 674.9 | 465.9 | 672.3 | 540.0 | 622.2 | 420.8 |
| Adrenals (pr) (G) | 0.040 | 0.072 | 0.059 | 0.050 | 0.048 | 0.080 | 0.070 | 0.080 | 0.063 |
| % BODY WEIGHT | 0.007 | 0.018 | 0.014 | 0.007 | 0.010 | 0.012 | 0.013 | 0.013 | 0.015 |
| Brain (G) | 2.220 | 1.993 | 2.141 | 1.870 | 2.213 | 2.220 | 2.290 | 1.980 | 2.105 |
| % BODY WEIGHT | 0.383 | 0.492 | 0.496 | 0.277 | 0.475 | 0.330 | 0.424 | 0.318 | 0.500 |
| Heart (G) | 1.780 | 1.316 | 1.474 | 1.720 | 1.464 | 1.760 | 1.650 | 1.740 | 1.829 |
| % BODY WEIGHT | 0.307 | 0.325 | 0.341 | 0.255 | 0.314 | 0.262 | 0.306 | 0.280 | 0.435 |
| Kidneys (pr) (G) | 4.750 | 3.394 | 3.507 | 4.100 | 4.693 | 4.670 | 3.940 | 4.650 | 4.049 |
| % BODY WEIGHT | 0.820 | 0.839 | 0.812 | 0.607 | 1.007 | 0.695 | 0.730 | 0.747 | 0.962 |
| Liver (G) | 21.600 | 13.535 | 16.183 | 18.200 | 18.796 | 26.760 | 16.160 | 22.640 | 16.780 |
| % BODY WEIGHT | 3.728 | 3.344 | 3.748 | 2.697 | 4.034 | 3.980 | 2.993 | 3.639 | 3.988 |
| Spleen (G) | 1.110 | 1.341 | 1.284 | 0.980 | 1.104 | 1.000 | 0.660 | 0.990 | 1.672 |
| % BODY WEIGHT | 0.192 | 0.331 | 0.297 | 0.145 | 0.237 | 0.149 | 0.122 | 0.159 | 0.397 |
| Testes w/Epidid. (pr) (G) | 5.670 | 2.616 | 5.136 | 5.070 | 4.921 | 4.930 | 4.550 | 5.780 | 4.689 |
| % BODY WEIGHT | 0.979 | 0.646 | 1.189 | 0.751 | 1.056 | 0.733 | 0.843 | 0.929 | 1.114 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 3M - 6.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| | | |
|---------------------------|--------|--------|
| ANIMAL ID: | 899 | 900 |
| BALANCE NO.: | | |
| BODY WEIGHT (G) | 500.7 | 596.6 |
| Adrenals (pr) (G) | 0.090 | 0.090 |
| % BODY WEIGHT | 0.018 | 0.015 |
| Brain (G) | 1.990 | 2.110 |
| % BODY WEIGHT | 0.397 | 0.354 |
| Heart (G) | 1.550 | 1.670 |
| % BODY WEIGHT | 0.310 | 0.280 |
| Kidneys (pr) (G) | 4.400 | 4.450 |
| % BODY WEIGHT | 0.879 | 0.746 |
| Liver (G) | 16.510 | 21.050 |
| % BODY WEIGHT | 3.297 | 3.528 |
| Spleen (G) | 0.680 | 0.700 |
| % BODY WEIGHT | 0.136 | 0.117 |
| Testes w/Epidid. (pr) (G) | 4.970 | 4.890 |
| % BODY WEIGHT | 0.993 | 0.820 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 4M - 18.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 922 | 923 | 924 | 925 | 927 | 928 | 929 | 930 | 931 |
|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| BODY WEIGHT (G) | 479.0 | 564.5 | 381.8 | 368.3 | 580.3 | 447.3 | 569.2 | 618.0 | 347.5 |
| Adrenals (pr) (G) | 0.080 | 0.050 | 0.057 | 0.053 | 0.070 | 0.085 | 0.090 | 0.080 | 0.031 |
| % BODY WEIGHT | 0.017 | 0.009 | 0.015 | 0.014 | 0.012 | 0.019 | 0.016 | 0.013 | 0.009 |
| Brain (G) | 2.110 | 2.070 | 2.061 | 2.102 | 2.310 | 2.154 | 2.180 | 2.020 | 1.826 |
| % BODY WEIGHT | 0.441 | 0.367 | 0.540 | 0.571 | 0.398 | 0.482 | 0.383 | 0.327 | 0.525 |
| Heart (G) | 1.920 | 1.610 | 1.521 | 1.652 | 1.890 | 1.875 | 1.850 | 1.950 | 1.415 |
| % BODY WEIGHT | 0.401 | 0.285 | 0.398 | 0.449 | 0.326 | 0.419 | 0.325 | 0.316 | 0.407 |
| Kidneys (pr) (G) | 4.290 | 3.850 | 4.814 | 3.957 | 4.440 | 4.046 | 4.880 | 4.020 | 4.020 |
| % BODY WEIGHT | 0.896 | 0.682 | 1.261 | 1.074 | 0.765 | 0.905 | 0.857 | 0.650 | 1.157 |
| Liver (G) | 17.780 | 15.420 | 18.141 | 17.124 | 17.010 | 18.354 | 21.800 | 20.950 | 14.496 |
| % BODY WEIGHT | 3.712 | 2.732 | 4.751 | 4.649 | 2.931 | 4.103 | 3.830 | 3.390 | 4.172 |
| Spleen (G) | 1.230 | 1.370 | 1.686 | 2.532 | 0.990 | 2.812 | 1.270 | 1.290 | 1.950 |
| % BODY WEIGHT | 0.257 | 0.243 | 0.442 | 0.687 | 0.171 | 0.629 | 0.223 | 0.209 | 0.561 |
| Testes w/Epidid. (pr) (G) | 5.680 | 5.320 | 5.127 | 4.819 | 5.160 | 6.167 | 5.930 | 4.890 | 4.904 |
| % BODY WEIGHT | 1.186 | 0.942 | 1.343 | 1.308 | 0.889 | 1.379 | 1.042 | 0.791 | 1.411 |

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: MALE

GROUP: 4M - 18.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 932 | 933 | 935 | 938 | 939 | 940 |
|----------------------------|--------|--------|--------|--------|--------|--------|
| BODY WEIGHT (G) | 521.2 | 565.8 | 512.8 | 376.7 | 523.0 | 589.4 |
| Adrenals (pr) (G) | 0.040 | 0.080 | 0.050 | 0.071 | 0.070 | 0.070 |
| % BODY WEIGHT | 0.008 | 0.014 | 0.010 | 0.019 | 0.013 | 0.012 |
| Brain (G) | 2.130 | 2.200 | 2.160 | 2.193 | 1.970 | 2.000 |
| % BODY WEIGHT | 0.409 | 0.389 | 0.421 | 0.582 | 0.377 | 0.339 |
| Heart (G) | 1.710 | 1.730 | 1.490 | 1.947 | 1.520 | 1.850 |
| % BODY WEIGHT | 0.328 | 0.306 | 0.291 | 0.517 | 0.291 | 0.314 |
| Kidneys (pr) (G) | 4.080 | 3.880 | 3.500 | 3.204 | 4.050 | 5.690 |
| % BODY WEIGHT | 0.783 | 0.686 | 0.683 | 0.851 | 0.774 | 0.965 |
| Liver (G) | 20.590 | 17.220 | 12.540 | 14.626 | 15.880 | 19.120 |
| % BODY WEIGHT | 3.950 | 3.043 | 2.445 | 3.883 | 3.036 | 3.244 |
| Spleen (G) | 1.300 | 1.530 | 0.880 | 2.309 | 1.310 | 1.300 |
| % BODY WEIGHT | 0.249 | 0.270 | 0.172 | 0.613 | 0.250 | 0.221 |
| Testes w/Epidid. (pr) (G) | 5.580 | 5.560 | 5.340 | 5.340 | 5.030 | 5.650 |
| % BODY WEIGHT | 1.071 | 0.983 | 1.041 | 1.418 | 0.962 | 0.959 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 1F - 0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 821 | 822 | 823 | 824 | 825 | 826 | 827 | 828 | 829 |
|----------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| BODY WEIGHT (G) | 269.3 | 258.0 | 315.5 | 293.1 | 258.6 | 294.4 | 278.0 | 293.1 | 240.9 |
| Adrenals (pr) (G) | 0.072 | 0.070 | 0.090 | 0.070 | 0.088 | 0.096 | 0.110 | 0.072 | 0.053 |
| % BODY WEIGHT | 0.027 | 0.027 | 0.029 | 0.024 | 0.034 | 0.033 | 0.040 | 0.025 | 0.022 |
| Brain (G) | 2.030 | 1.947 | 2.170 | 2.050 | 2.038 | 2.048 | 2.110 | 1.907 | 1.969 |
| % BODY WEIGHT | 0.754 | 0.755 | 0.688 | 0.699 | 0.788 | 0.696 | 0.759 | 0.651 | 0.817 |
| Heart (G) | 0.864 | 0.855 | 1.130 | 0.960 | 0.919 | 0.964 | 1.010 | 0.949 | 0.917 |
| % BODY WEIGHT | 0.321 | 0.331 | 0.358 | 0.328 | 0.355 | 0.327 | 0.363 | 0.324 | 0.381 |
| Kidneys (pr) (G) | 2.158 | 1.933 | 2.080 | 2.230 | 2.237 | 2.316 | 2.220 | 2.190 | 2.187 |
| % BODY WEIGHT | 0.801 | 0.749 | 0.659 | 0.761 | 0.865 | 0.787 | 0.799 | 0.747 | 0.908 |
| Liver (G) | 9.884 | 7.411 | 9.470 | 7.720 | 8.736 | 9.769 | 8.860 | 8.885 | 7.549 |
| % BODY WEIGHT | 3.670 | 2.872 | 3.002 | 2.634 | 3.378 | 3.318 | 3.187 | 3.031 | 3.134 |
| Ovaries (G) | 0.111 | 0.126 | 0.090 | 0.080 | 0.121 | 0.170 | 0.120 | 0.143 | 0.104 |
| % BODY WEIGHT | 0.041 | 0.049 | 0.029 | 0.027 | 0.047 | 0.058 | 0.043 | 0.049 | 0.043 |
| Spleen (G) | 0.582 | 0.394 | 0.480 | 0.450 | 0.729 | 0.525 | 0.590 | 0.543 | 0.459 |
| % BODY WEIGHT | 0.216 | 0.153 | 0.152 | 0.154 | 0.282 | 0.178 | 0.212 | 0.185 | 0.191 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 1F - 0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 830 | 831 | 832 | 833 | 834 | 835 | 836 | 837 | 838 |
|----------------------------|-------|-------|-------|-------|-------|--------|-------|-------|--------|
| BODY WEIGHT (G) | 324.5 | 284.9 | 250.9 | 289.4 | 328.5 | 366.0 | 337.3 | 328.8 | 278.1 |
| Adrenals (pr) (G) | 0.110 | 0.050 | 0.067 | 0.070 | 0.080 | 0.070 | 0.070 | 0.070 | 0.076 |
| % BODY WEIGHT | 0.034 | 0.018 | 0.027 | 0.024 | 0.024 | 0.019 | 0.021 | 0.021 | 0.027 |
| Brain (G) | 1.990 | 1.860 | 2.010 | 1.916 | 1.960 | 2.000 | 2.110 | 1.860 | 2.139 |
| % BODY WEIGHT | 0.613 | 0.653 | 0.801 | 0.662 | 0.597 | 0.546 | 0.626 | 0.566 | 0.769 |
| Heart (G) | 1.370 | 1.070 | 1.132 | 0.960 | 1.120 | 1.090 | 1.120 | 1.060 | 1.060 |
| % BODY WEIGHT | 0.422 | 0.376 | 0.451 | 0.332 | 0.341 | 0.298 | 0.332 | 0.322 | 0.381 |
| Kidneys (pr) (G) | 2.220 | 2.110 | 1.896 | 1.920 | 2.190 | 2.170 | 2.280 | 2.570 | 2.233 |
| % BODY WEIGHT | 0.684 | 0.741 | 0.756 | 0.663 | 0.667 | 0.593 | 0.676 | 0.782 | 0.803 |
| Liver (G) | 9.880 | 8.240 | 8.267 | 7.607 | 8.710 | 10.000 | 9.840 | 9.190 | 10.232 |
| % BODY WEIGHT | 3.045 | 2.892 | 3.295 | 2.629 | 2.651 | 2.732 | 2.917 | 2.795 | 3.679 |
| Ovaries (G) | 0.110 | 0.090 | 0.120 | 0.117 | 0.100 | 0.130 | 0.130 | 0.130 | 0.112 |
| % BODY WEIGHT | 0.034 | 0.032 | 0.048 | 0.040 | 0.030 | 0.036 | 0.039 | 0.040 | 0.040 |
| Spleen (G) | 0.500 | 0.450 | 0.491 | 0.467 | 0.450 | 0.570 | 0.620 | 0.530 | 0.500 |
| % BODY WEIGHT | 0.154 | 0.158 | 0.196 | 0.161 | 0.137 | 0.156 | 0.184 | 0.161 | 0.180 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 1F - 0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 839 | 840 |
|----------------------------|-------|-------|
| BODY WEIGHT (G) | 304.3 | 281.7 |
| Adrenals (pr) (G) | 0.052 | 0.100 |
| % BODY WEIGHT | 0.017 | 0.035 |
| Brain (G) | 1.991 | 2.010 |
| % BODY WEIGHT | 0.654 | 0.714 |
| Heart (G) | 1.049 | 1.190 |
| % BODY WEIGHT | 0.345 | 0.422 |
| Kidneys (pr) (G) | 2.249 | 2.340 |
| % BODY WEIGHT | 0.739 | 0.831 |
| Liver (G) | 9.243 | 8.760 |
| % BODY WEIGHT | 3.037 | 3.110 |
| Ovaries (G) | 0.088 | 0.110 |
| % BODY WEIGHT | 0.029 | 0.039 |
| Spleen (G) | 0.590 | 0.460 |
| % BODY WEIGHT | 0.194 | 0.163 |

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 2F - 0.5 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 861 | 862 | 863 | 864 | 865 | 866 | 867 | 868 | 869 |
|----------------------------|--------|-------|-------|--------|-------|-------|-------|-------|-------|
| BODY WEIGHT (G) | 348.6 | 258.8 | 248.3 | 287.8 | 246.6 | 272.6 | 343.6 | 281.6 | 298.4 |
| Adrenals (pr) (G) | 0.090 | 0.061 | 0.089 | 0.110 | 0.060 | 0.062 | 0.090 | 0.080 | 0.064 |
| % BODY WEIGHT | 0.026 | 0.024 | 0.036 | 0.038 | 0.024 | 0.023 | 0.026 | 0.028 | 0.021 |
| Brain (G) | 2.200 | 1.739 | 2.079 | 1.970 | 2.105 | 1.861 | 1.810 | 1.910 | 2.020 |
| % BODY WEIGHT | 0.631 | 0.672 | 0.837 | 0.685 | 0.854 | 0.683 | 0.527 | 0.678 | 0.677 |
| Heart (G) | 1.210 | 0.897 | 0.789 | 1.170 | 1.012 | 0.972 | 1.110 | 1.150 | 0.919 |
| % BODY WEIGHT | 0.347 | 0.347 | 0.318 | 0.407 | 0.410 | 0.357 | 0.323 | 0.408 | 0.308 |
| Kidneys (pr) (G) | 2.800 | 1.963 | 1.976 | 2.200 | 2.157 | 2.174 | 2.530 | 2.190 | 2.328 |
| % BODY WEIGHT | 0.803 | 0.759 | 0.796 | 0.764 | 0.875 | 0.798 | 0.736 | 0.778 | 0.780 |
| Liver (G) | 10.740 | 7.425 | 8.043 | 10.130 | 8.102 | 9.193 | 9.290 | 8.090 | 9.377 |
| % BODY WEIGHT | 3.081 | 2.869 | 3.239 | 3.520 | 3.285 | 3.372 | 2.704 | 2.873 | 3.142 |
| Ovaries (G) | 0.090 | 0.128 | 0.128 | 0.110 | 0.187 | 0.129 | 0.120 | 0.070 | 0.157 |
| % BODY WEIGHT | 0.026 | 0.049 | 0.052 | 0.038 | 0.076 | 0.047 | 0.035 | 0.025 | 0.053 |
| Spleen (G) | 0.440 | 0.589 | 0.449 | 0.520 | 0.477 | 0.556 | 0.620 | 0.390 | 0.865 |
| % BODY WEIGHT | 0.126 | 0.228 | 0.181 | 0.181 | 0.193 | 0.204 | 0.180 | 0.138 | 0.290 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 2F - 0.5 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 870 | 871 | 872 | 873 | 874 | 875 | 876 | 877 | 878 |
|----------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| BODY WEIGHT (G) | 255.3 | 254.8 | 287.9 | 297.2 | 326.3 | 273.0 | 271.0 | 319.8 | 296.9 |
| Adrenals (pr) (G) | 0.072 | 0.090 | 0.086 | 0.060 | 0.100 | 0.097 | 0.101 | 0.080 | 0.049 |
| % BODY WEIGHT | 0.028 | 0.035 | 0.030 | 0.020 | 0.031 | 0.036 | 0.037 | 0.025 | 0.017 |
| Brain (G) | 2.103 | 1.950 | 1.934 | 2.060 | 1.890 | 1.992 | 2.040 | 1.960 | 1.913 |
| % BODY WEIGHT | 0.824 | 0.765 | 0.672 | 0.693 | 0.579 | 0.730 | 0.753 | 0.613 | 0.644 |
| Heart (G) | 0.831 | 0.850 | 0.890 | 1.040 | 1.120 | 1.074 | 0.952 | 1.160 | 0.993 |
| % BODY WEIGHT | 0.326 | 0.334 | 0.309 | 0.350 | 0.343 | 0.393 | 0.351 | 0.363 | 0.334 |
| Kidneys (pr) (G) | 2.078 | 1.840 | 1.873 | 2.050 | 2.180 | 2.252 | 2.373 | 2.080 | 1.941 |
| % BODY WEIGHT | 0.814 | 0.722 | 0.651 | 0.690 | 0.668 | 0.825 | 0.876 | 0.650 | 0.654 |
| Liver (G) | 8.108 | 7.770 | 7.919 | 7.660 | 8.650 | 9.211 | 9.427 | 9.310 | 8.221 |
| % BODY WEIGHT | 3.176 | 3.049 | 2.751 | 2.577 | 2.651 | 3.374 | 3.479 | 2.911 | 2.769 |
| Ovaries (G) | 0.102 | 0.090 | 0.153 | 0.100 | 0.170 | 0.120 | 0.128 | 0.090 | 0.090 |
| % BODY WEIGHT | 0.040 | 0.035 | 0.053 | 0.034 | 0.052 | 0.044 | 0.047 | 0.028 | 0.030 |
| Spleen (G) | 0.456 | 0.580 | 0.513 | 0.460 | 0.520 | 0.443 | 0.576 | 0.450 | 0.594 |
| % BODY WEIGHT | 0.179 | 0.228 | 0.178 | 0.155 | 0.159 | 0.162 | 0.213 | 0.141 | 0.200 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 2F - 0.5 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 879 | 880 |
|----------------------------|-------|--------|
| BODY WEIGHT (G) | 266.9 | 368.2 |
| Adrenals (pr) (G) | 0.050 | 0.070 |
| % BODY WEIGHT | 0.019 | 0.019 |
| Brain (G) | 1.950 | 2.030 |
| % BODY WEIGHT | 0.731 | 0.551 |
| Heart (G) | 0.980 | 1.140 |
| % BODY WEIGHT | 0.367 | 0.310 |
| Kidneys (pr) (G) | 1.990 | 2.510 |
| % BODY WEIGHT | 0.746 | 0.682 |
| Liver (G) | 6.980 | 10.710 |
| % BODY WEIGHT | 2.615 | 2.909 |
| Ovaries (G) | 0.090 | 0.110 |
| % BODY WEIGHT | 0.034 | 0.030 |
| Spleen (G) | 0.540 | 0.610 |
| % BODY WEIGHT | 0.202 | 0.166 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 3F - 6.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 901 | 902 | 903 | 904 | 905 | 906 | 907 | 908 | 909 |
|----------------------------|-------|-------|-------|-------|-------|-------|-------|--------|--------|
| BODY WEIGHT (G) | 295.1 | 273.8 | 255.7 | 327.0 | 255.7 | 223.8 | 246.7 | 297.0 | 317.4 |
| Adrenals (pr) (G) | 0.090 | 0.070 | 0.084 | 0.090 | 0.119 | 0.079 | 0.084 | 0.100 | 0.070 |
| % BODY WEIGHT | 0.030 | 0.026 | 0.033 | 0.028 | 0.047 | 0.035 | 0.034 | 0.034 | 0.022 |
| Brain (G) | 2.010 | 2.010 | 1.986 | 2.090 | 1.969 | 1.865 | 1.940 | 2.130 | 2.030 |
| % BODY WEIGHT | 0.681 | 0.734 | 0.777 | 0.639 | 0.770 | 0.833 | 0.786 | 0.717 | 0.640 |
| Heart (G) | 1.010 | 0.970 | 1.062 | 1.110 | 0.874 | 0.810 | 0.942 | 1.180 | 1.040 |
| % BODY WEIGHT | 0.342 | 0.354 | 0.415 | 0.339 | 0.342 | 0.362 | 0.382 | 0.397 | 0.328 |
| Kidneys (pr) (G) | 2.450 | 2.010 | 2.451 | 2.330 | 2.250 | 2.140 | 2.316 | 2.660 | 2.360 |
| % BODY WEIGHT | 0.830 | 0.734 | 0.959 | 0.713 | 0.880 | 0.956 | 0.939 | 0.896 | 0.744 |
| Liver (G) | 8.590 | 7.990 | 9.119 | 9.840 | 9.594 | 7.899 | 8.467 | 11.000 | 10.120 |
| % BODY WEIGHT | 2.911 | 2.918 | 3.566 | 3.009 | 3.752 | 3.529 | 3.432 | 3.704 | 3.188 |
| Ovaries (G) | 0.090 | 0.140 | 0.198 | 0.120 | 0.173 | 0.132 | 0.142 | 0.090 | 0.140 |
| % BODY WEIGHT | 0.030 | 0.051 | 0.077 | 0.037 | 0.068 | 0.059 | 0.058 | 0.030 | 0.044 |
| Spleen (G) | 0.640 | 0.560 | 0.884 | 0.570 | 0.844 | 0.589 | 1.106 | 0.530 | 0.500 |
| % BODY WEIGHT | 0.217 | 0.205 | 0.346 | 0.174 | 0.330 | 0.263 | 0.448 | 0.178 | 0.158 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 3F - 6.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 910 | 911 | 912 | 913 | 914 | 915 | 916 | 917 | 918 |
|----------------------------|-------|-------|--------|-------|-------|-------|-------|-------|-------|
| BODY WEIGHT (G) | 255.5 | 256.4 | 320.9 | 268.4 | 243.2 | 276.4 | 305.5 | 237.6 | 283.8 |
| Adrenals (pr) (G) | 0.097 | 0.087 | 0.110 | 0.072 | 0.095 | 0.080 | 0.100 | 0.054 | 0.070 |
| % BODY WEIGHT | 0.038 | 0.034 | 0.034 | 0.027 | 0.039 | 0.029 | 0.033 | 0.023 | 0.025 |
| Brain (G) | 1.919 | 1.987 | 1.900 | 1.950 | 1.998 | 1.970 | 2.060 | 1.920 | 1.980 |
| % BODY WEIGHT | 0.751 | 0.775 | 0.592 | 0.727 | 0.822 | 0.713 | 0.674 | 0.808 | 0.698 |
| Heart (G) | 0.922 | 0.981 | 0.990 | 0.962 | 0.829 | 0.980 | 1.180 | 0.842 | 0.980 |
| % BODY WEIGHT | 0.361 | 0.383 | 0.309 | 0.358 | 0.341 | 0.355 | 0.386 | 0.354 | 0.345 |
| Kidneys (pr) (G) | 2.617 | 2.208 | 2.650 | 2.359 | 2.173 | 1.930 | 2.130 | 2.261 | 2.010 |
| % BODY WEIGHT | 1.024 | 0.861 | 0.826 | 0.879 | 0.894 | 0.698 | 0.697 | 0.952 | 0.708 |
| Liver (G) | 8.905 | 9.326 | 11.940 | 9.917 | 9.155 | 8.090 | 9.420 | 8.373 | 8.200 |
| % BODY WEIGHT | 3.485 | 3.637 | 3.721 | 3.695 | 3.764 | 2.927 | 3.083 | 3.524 | 2.889 |
| Ovaries (G) | 0.139 | 0.176 | 0.120 | 0.158 | 0.140 | 0.080 | 0.120 | 0.107 | 0.060 |
| % BODY WEIGHT | 0.054 | 0.069 | 0.037 | 0.059 | 0.058 | 0.029 | 0.039 | 0.045 | 0.021 |
| Spleen (G) | 0.721 | 0.942 | 0.550 | 0.889 | 0.647 | 0.540 | 0.550 | 0.752 | 0.520 |
| % BODY WEIGHT | 0.282 | 0.367 | 0.171 | 0.331 | 0.266 | 0.195 | 0.180 | 0.316 | 0.183 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

DRAFT

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 3F - 6.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 919 | 920 |
|----------------------------|-------|-------|
| BODY WEIGHT (G) | 308.8 | 254.5 |
| Adrenals (pr) (G) | 0.060 | 0.071 |
| % BODY WEIGHT | 0.019 | 0.028 |
| Brain (G) | 2.150 | 1.937 |
| % BODY WEIGHT | 0.696 | 0.761 |
| Heart (G) | 1.030 | 1.019 |
| % BODY WEIGHT | 0.334 | 0.400 |
| Kidneys (pr) (G) | 2.370 | 2.234 |
| % BODY WEIGHT | 0.767 | 0.878 |
| Liver (G) | 9.070 | 9.178 |
| % BODY WEIGHT | 2.937 | 3.606 |
| Ovaries (G) | 0.150 | 0.108 |
| % BODY WEIGHT | 0.049 | 0.042 |
| Spleen (G) | 0.560 | 0.669 |
| % BODY WEIGHT | 0.181 | 0.263 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

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INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 4F - 18.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 941 | 942 | 943 | 944 | 945 | 946 | 947 | 948 | 949 |
|----------------------------|-------|-------|-------|--------|-------|--------|-------|--------|-------|
| BODY WEIGHT (G) | 278.3 | 272.1 | 247.3 | 305.3 | 227.7 | 262.8 | 227.5 | 242.9 | 268.8 |
| Adrenals (pr) (G) | 0.080 | 0.050 | 0.106 | 0.070 | 0.088 | 0.087 | 0.107 | 0.079 | 0.040 |
| % BODY WEIGHT | 0.029 | 0.018 | 0.043 | 0.023 | 0.039 | 0.033 | 0.047 | 0.033 | 0.015 |
| Brain (G) | 1.830 | 1.920 | 2.009 | 2.170 | 1.811 | 2.076 | 1.934 | 1.943 | 1.910 |
| % BODY WEIGHT | 0.658 | 0.706 | 0.812 | 0.711 | 0.795 | 0.790 | 0.850 | 0.800 | 0.711 |
| Heart (G) | 1.050 | 1.090 | 0.836 | 1.090 | 0.926 | 1.062 | 0.931 | 1.289 | 0.950 |
| % BODY WEIGHT | 0.377 | 0.401 | 0.338 | 0.357 | 0.407 | 0.404 | 0.409 | 0.531 | 0.353 |
| Kidneys (pr) (G) | 2.480 | 2.180 | 2.021 | 2.660 | 2.165 | 2.505 | 2.061 | 2.198 | 1.920 |
| % BODY WEIGHT | 0.891 | 0.801 | 0.817 | 0.871 | 0.951 | 0.953 | 0.906 | 0.905 | 0.714 |
| Liver (G) | 9.500 | 7.690 | 9.116 | 10.210 | 8.668 | 10.296 | 9.318 | 10.550 | 8.030 |
| % BODY WEIGHT | 3.414 | 2.826 | 3.686 | 3.344 | 3.807 | 3.918 | 4.096 | 4.343 | 2.987 |
| Ovaries (G) | 0.040 | 0.110 | 0.207 | 0.110 | 0.118 | 0.209 | 0.163 | 0.113 | 0.090 |
| % BODY WEIGHT | 0.014 | 0.040 | 0.084 | 0.036 | 0.052 | 0.080 | 0.072 | 0.047 | 0.033 |
| Spleen (G) | 0.940 | 0.700 | 1.089 | 0.930 | 1.332 | 1.645 | 1.339 | 1.946 | 0.880 |
| % BODY WEIGHT | 0.338 | 0.257 | 0.440 | 0.305 | 0.585 | 0.626 | 0.589 | 0.801 | 0.327 |

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALE

GROUP: 4F - 18.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCES

| ANIMAL ID: BALANCE NO.: | 950 | 951 | 952 | 953 | 954 | 955 | 957 | 958 | 959 |
|----------------------------|--------|--------|-------|-------|-------|--------|-------|-------|--------|
| BODY WEIGHT (G) | 242.8 | 225.1 | 222.1 | 306.3 | 297.1 | 247.0 | 305.1 | 217.8 | 310.0 |
| Adrenals (pr) (G) | 0.086 | 0.087 | 0.082 | 0.100 | 0.090 | 0.098 | 0.080 | 0.064 | 0.090 |
| % BODY WEIGHT | 0.035 | 0.039 | 0.037 | 0.033 | 0.030 | 0.040 | 0.026 | 0.029 | 0.029 |
| Brain (G) | 1.895 | 1.908 | 1.810 | 2.020 | 2.060 | 1.903 | 2.020 | 1.943 | 1.990 |
| % BODY WEIGHT | 0.780 | 0.848 | 0.815 | 0.659 | 0.693 | 0.770 | 0.662 | 0.892 | 0.642 |
| Heart (G) | 0.952 | 0.930 | 0.871 | 1.060 | 1.100 | 1.061 | 1.240 | 0.784 | 1.070 |
| % BODY WEIGHT | 0.392 | 0.413 | 0.392 | 0.346 | 0.370 | 0.430 | 0.406 | 0.360 | 0.345 |
| Kidneys (pr) (G) | 2.324 | 2.751 | 2.074 | 2.500 | 2.800 | 2.707 | 2.700 | 1.954 | 2.980 |
| % BODY WEIGHT | 0.957 | 1.222 | 0.934 | 0.816 | 0.942 | 1.096 | 0.885 | 0.897 | 0.961 |
| Liver (G) | 10.524 | 10.060 | 9.099 | 9.340 | 9.330 | 10.414 | 8.240 | 7.894 | 10.770 |
| % BODY WEIGHT | 4.334 | 4.469 | 4.097 | 3.049 | 3.140 | 4.216 | 2.701 | 3.624 | 3.474 |
| Ovaries (G) | 0.131 | 0.169 | 0.177 | 0.150 | 0.110 | 0.162 | 0.130 | 0.104 | 0.100 |
| % BODY WEIGHT | 0.054 | 0.075 | 0.080 | 0.049 | 0.037 | 0.066 | 0.043 | 0.048 | 0.032 |
| Spleen (G) | 1.406 | 1.228 | 1.333 | 0.700 | 0.910 | 1.545 | 0.720 | 1.160 | 0.700 |
| % BODY WEIGHT | 0.579 | 0.546 | 0.600 | 0.229 | 0.306 | 0.626 | 0.236 | 0.533 | 0.226 |

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 098
SEX: FEMALEGROUP: 4F - 18.0 mg base/kg/day
ALL FATES ALL DAYS ALL BALANCESANIMAL ID: 960
BALANCE NO.:

| | |
|-------------------|-------|
| BODY WEIGHT (G) | 256.8 |
| Adrenals (pr) (G) | 0.110 |
| % BODY WEIGHT | 0.043 |
| Brain (G) | 1.970 |
| % BODY WEIGHT | 0.767 |
| Heart (G) | 1.200 |
| % BODY WEIGHT | 0.467 |
| Kidneys (pr) (G) | 2.310 |
| % BODY WEIGHT | 0.900 |
| Liver (G) | 7.670 |
| % BODY WEIGHT | 2.987 |
| Ovaries (G) | 0.080 |
| % BODY WEIGHT | 0.031 |
| Spleen (G) | 0.610 |
| % BODY WEIGHT | 0.238 |

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APPENDIX 10
Pathology Report

DRAFT PATHOLOGY REPORT FOR
TRL STUDY NUMBER 098
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

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SEPTEMBER 28, 1993

TABLE OF CONTENTS

| SECTION | TITLE | PAGE |
|---------|---|------|
| I | Pathology Narrative | 3 |
| | Summary of Experimental Design (Table I) | 10 |
| | Protocol-Required Tissues (Table II) | 10 |
| | Tissue Accountability Record (Table III) | 11 |
| | Report Codes Table | 12 |
| | Abbreviation List | 13 |
| II | Project Summary Table | 14 |
| | Males | 15 |
| | Females | 19 |
| III | Severity Summary Table | 24 |
| | Males | 25 |
| | Females | 29 |
| IV | Tabulated Animal Data | 33 |
| | Males | 34 |
| | Females | 49 |
| V | Correlation of Gross and Microscopic (Micro) Findings | 68 |
| | Males | 69 |
| | Females | 95 |
| VI | Quality Assurance Statement | 122 |
| VII | Appendix 1: Bone Marrow Report | 124 |

SECTION I
PATHOLOGY NARRATIVE

DRAFT PATHOLOGY REPORT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INTRODUCTION

This pathology report, submitted by Pathology Associates, Inc. (PAI) to Toxicology Research Laboratory (TRL), represents the pathology findings for the study designated as "Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats," TRL Study Number 098.

EXPERIMENTAL DESIGN AND METHODS

Three groups, each composed of male and female CD® (Virus Antibody Free) rats, were given the test article (WR238605) once daily by gavage for at least 13 weeks, starting with Day 0. Dose levels administered are shown in the Summary of Experimental Design (Table I). A control group of male and female rats was included, and received test article vehicle (aqueous 1% methylcellulose/0.4% Tween 80) by gavage for at least 13 weeks, starting with Day 0. Animals designated for sacrifice at the end of the 13 week dosing period were dosed up to and including the day prior to their scheduled sacrifice and necropsy on Days 91 and 92 (study week 14). Designated recovery animals were dosed for 91 days and then held for a 13 week recovery period before being sacrificed and necropsied at the beginning of study week 27. Scheduled necropsies were performed according to TRL Standard Operating Procedures under the supervision of Ralph M. Bunte, DVM.

Tissues required by the protocol, except as noted in the Tissue Accountability Record (Table III), were processed in accordance with PAI Standard Operating Procedures. Protocol-required tissues from control and high dose animals sacrificed at the end of dosing were evaluated by light microscopy. Results of this evaluation were summarized, and pituitary gland, thyroid gland, liver, spleen, lung, kidney, and bone marrow were identified as potential target organs. These tissues from low and middle dose groups sacrificed at the end of dosing, and from control and high dose recovery groups, were then processed. The potential target organs from these animals were evaluated/ re-evaluated by light microscopy. When necessary, in order to resolve discrepancies in evaluation, slides were randomized and examined without knowledge of treatment group or sex. Following these evaluations, lung, kidney, bone marrow, and spleen were identified as target organs. Lungs from low and middle dose recovery groups were then processed and examined microscopically in order to evaluate test article-related effects seen in the lungs of high dose recovery group animals.

Most tissues that were not accounted for were from animals that died during the study. No test article-related changes occurred in mammary gland, parathyroid gland, pituitary gland, diaphragm, or costochondral junction. For this reason, the unaccountability of the few tissues missing from terminal sacrifice animals is believed not to have affected the outcome of the study.

Microscopic findings for terminal sacrifice animals from all groups are summarized in the Project Summary Tables (Section II). The mean group severity scores for these animals are found in the Severity Summary Tables (Section III). The mean group severity scores were determined by dividing the sum of all severity scores for a finding by the number of tissues examined. Microscopic findings in the protocol-required tissues for individual animals are presented in the Tabulated Animal Data Tables (Section IV). The correlation of the necropsy findings and histopathology findings are reported in the Correlation of Gross and Microscopic (Micro) Findings (Section V). The codes used as entries in these tables are explained in the Report Codes Table. Abbreviations used in these tables are explained in the Abbreviation List.

RESULTS AND DISCUSSION

The Results and Discussion section is divided into four parts: Unscheduled Deaths, Gross Lesions, Diagnostic Terms, and Histopathology Findings. The Diagnostic Terms portion lists and clarifies diagnostic terminology that may be unclear. Terms listed in the Diagnostic Terms portion of this section were not necessarily considered to be test article-related. The Histopathology Findings portion of this section reports the results and provides discussion of the histopathologic evaluation of the tissues.

Unscheduled Deaths

Five high dose group males died prior to the end of dosing, during weeks 2 (#0921, #0926, #0936, and #0937) and 8 (#0934). The cause of death for each of the four animals that died during week 2 could not be determined. Each of these animals had inflammation in the structures of the thoracic cavity or multifocal inflammation consistent with septicemia when tissues from these animals were evaluated microscopically. However, no injuries, such as esophageal lacerations, that would explain the inflammation were found during review of tissues from these animals. Also, microscopic changes that were found to be test article-related in animals sacrificed at the end of dosing were not present in these animals. Microscopic evaluation of tissues from animal #0934 revealed alveolar proteinosis in the lung, hemoglobin nephrosis, and renal hemosiderosis. These were found to be test article-related changes in animals sacrificed at the end of dosing. For these reasons, the death of animal #0934 was attributed to the test article. One high dose group female (#0956) died following CO₂ anesthesia for blood collection (per Study Director) during the recovery period (week 16).

Gross Lesions

Potentially treatment-related gross lesions were identified in the lungs of middle and high dose rats sacrificed at the end of dosing and after the recovery period. The lesions were morphologically consistent in all animals in which they occurred. They were described as multiple, irregular, white lesions on the pleura, which varied from focal to linear.

Diagnostic Terms

The morphologic characteristics of observations and lesions which require comment are presented in subsequent paragraphs to aid in the interpretation of the data.

Lung

Alveolar proteinosis consisted of two distinct components. First, there was pale, eosinophilic, amorphous to fibrillar material within alveoli. The second feature was discrete, large, round to oval cells which had abundant vacuolated cytoplasm. These cells were free in the lumina of alveoli and terminal bronchioles but did not appear to line alveolar septa. Occasionally, a few neutrophils were also present.

Chronic inflammation was seen in animals sacrificed after the recovery period. It was usually focal and subpleural. It consisted of interstitial fibrosis, mononuclear cell infiltration, and sometimes hyperplasia of alveolar and bronchiolar epithelium. Cholesterol clefts were also present in many of these foci.

In recovery animals, there were clusters of macrophages filling randomly scattered alveoli. These cells contained variable cytoplasmic granules that were positive for iron by Perl's stain and were non-acid-fast. These granules were identified as hemosiderin. Hemosiderin can be distinguished

from lipofuscin by iron and acid-fast stains. Hemosiderin is iron (Perl's stain) positive and acid-fast negative, while lipofuscin is iron negative and acid-fast positive.

Kidney

Hemoglobin nephrosis was characterized by proteinic droplets in the lumen of renal tubules and by degenerative changes in the tubular epithelium. The degenerative changes in tubular epithelium consisted of irregularly scalloped luminal cell borders, proteinic cytoplasmic droplets, cytoplasmic vacuolation, and necrosis.

Hemosiderin was deposited as variably-sized golden-brown granules in the cytoplasm of tubular epithelial cells.

Spleen

Hyperplasia of the spleen consisted of an increase in normal cellular components in the spleen. This resulted in sections of spleen that appeared histologically normal except for an increased cross-sectional size.

Bone Marrow

Hemosiderin deposition in the bone marrow consisted of golden-brown granules in macrophages in the histologic sections of bone marrow.

The remainder of the diagnoses used in this study were considered to be self-explanatory and were not discussed in this section.

Histopathology Findings

Lung

Among animals sacrificed at the end of dosing, alveolar proteinosis was diagnosed in 0 out of 10, 0 out of 10, 10 out of 10, and 5 out of 5 males, and in 0 out of 10, 0 out of 10, 10 out of 10, and 10 out of 10 females in the control, low, middle, and high dose groups, respectively. Mean group severity scores for this change were 0.00, 0.00, 1.70, and 2.80 in males, and 0.00, 0.00, 1.60, and 2.20 in females in the control, low, middle, and high dose groups, respectively. Alveolar proteinosis did not occur in males or in females sacrificed after the recovery period. The incidence and mean group severity scores for alveolar proteinosis in animals sacrificed at the end of dosing were interpreted as consistent with a dose-related response. This observation, in conjunction with resolution of this change in animals sacrificed after the recovery period, indicates alveolar proteinosis to be a test article-related change. This lesion corresponded to the gross lesions described in the lungs of middle and high dose animals sacrificed at the end of dosing.

Chronic inflammation in the lung was observed only in animals sacrificed after the recovery period. In recovery males, this change occurred in 0 out of 10, 0 out of 10, 5 out of 10, and 1 out of 10 animals in the control, low, middle, and high dose groups, with mean group severity scores of 0.00, 0.00, 0.50, and 0.20, respectively. In recovery females, this change occurred in 0 out of 10, 0 out of 10, 7 out of 10, and 5 out of 9 animals in the control, low, middle, and high dose groups, with mean group severity scores of 0.00, 0.00, 1.10, and 0.67, respectively. Chronic inflammation was focal or multifocal, randomly distributed, usually subpleural, and not always associated with gross lesions (see Gross Lesions). For these reasons, the observation of chronic inflammation in a single 5-6 micron thick section of lung was fortuitous. These observations account for the lack of a dose-related incidence and the low mean group severity scores for this change. A possible relationship between chronic inflammation and alveolar proteinosis in the lung is speculative, as these changes occurred at different points in time. Such a relationship seems likely, however, as alveolar proteinosis had resolved by the end of the recovery period, and no other change that would have resulted in chronic inflammation of the lung was noted in animals

sacrificed at the end of dosing. For these reasons, chronic inflammation in the lungs of recovery animals was interpreted as part of the resolution of alveolar proteinosis and was, thus, secondary to a direct test article-related effect.

Deposition of hemosiderin pigment occurred in 1 out of 10 control males sacrificed at the end of dosing, with a mean group severity score of 0.20. This hemosiderin was associated with an area of previous hemorrhage in alveoli. Among animals sacrificed after the recovery period, hemosiderin deposition in the lung occurred in 1 out of 10, 7 out of 10, and 8 out of 10 males, and in 0 out of 10, 8 out of 10, and 9 out of 9 females in the low, middle, and high dose groups, respectively. Mean group severity scores for this change in these animals were 0.10, 0.80, and 0.80 in males, and 0.00, 1.20, and 1.11 in females in the low, middle, and high dose groups, respectively. This change did not occur in the lungs of control males or females sacrificed after the recovery period. The hemosiderin in the lung of the low dose male sacrificed after the recovery period was in the interstitium rather than the alveoli. For this reason, the hemosiderin in this animal was considered unrelated to the hemosiderin which occurred in alveoli of middle and high dose group recovery animals. The hemosiderin in alveoli of the lungs of middle and high dose group recovery animals was initially thought to be lipofuscin. Staining selected lungs with Perl's stain and an acid-fast stain confirmed the pigment to be hemosiderin rather than lipofuscin. In view of changes in the kidneys (discussed below), this hemosiderin most likely resulted from the presence of hemoglobin in the proteinic material seen in alveolar proteinosis. Alveolar macrophages, as part of the resolution of alveolar proteinosis, phagocytized this hemoglobin and processed it to hemosiderin. These clusters of hemosiderin-laden macrophages had not yet been able to clear out of the lung at the time of the recovery sacrifice. For these reasons, hemosiderin in alveolar macrophages was also interpreted as secondary to a direct test article-related effect.

The changes described as alveolar proteinosis in the lungs of these rats are similar to those described as alveolar proteinosis in the Fischer 344 rat. The causes for alveolar proteinosis in the rat are not known, but altered vascular permeability and abnormal surfactant production and degradation have been suggested.¹ These changes are also similar to changes related to chronic pulmonary edema in domestic animals.² Altered vascular permeability as the mechanism for alveolar proteinosis is also suggested by hemosiderin in alveolar macrophages in recovery rats. Fragments of cell membrane from lysed erythrocytes could also have passed into alveoli and contributed to the cholesterol clefts in the chronic inflammation. This would further support increased vascular permeability as the cause of alveolar proteinosis. For these reasons, and due to incidence and mean group severity scores at the end of dosing and after the recovery period, alveolar proteinosis, chronic inflammation, and hemosiderin in alveolar macrophages were considered pathophysiologically-related processes. Alveolar proteinosis was interpreted as a direct test article-related effect, while chronic inflammation and hemosiderin deposits were secondary test article-related effects representing resolution of the alveolar proteinosis.

Kidney

Hemoglobin nephrosis occurred in middle and high dose animals sacrificed at the end of dosing. This change did not occur in control or low dose animals sacrificed at the end of dosing or in control and high dose recovery animals. Among animals sacrificed at the end of dosing, hemoglobin nephrosis occurred in 5 out of 10 and 5 out of 5 males, and in 4 out of 10 and 10 out of 10 females in the middle and high dose groups, respectively. Mean group severity scores for

¹ G.A. Boorman and S.L. Eustis, "Lung," Pathology of the Fischer Rat, Reference and Atlas, eds. G.A. Boorman, S.L. Eustis, M.R. Elwell, C.A. Montgomery, Jr., and W.F. MacKenzie, (San Diego: Academic Press, Inc., 1990), pp. 345-346.

² D.L. Dungworth, "Respiratory System," Pathology of Domestic Animals, eds. K.V.F. Jubb, P.C. Kennedy, and N. Palmer, (San Diego: Academic Press, Inc., 1985), pp. 407-448.

this change were 0.50 and 2.20 in males, and 0.40 and 1.50 in females in the middle and high dose groups, respectively.

Hemosiderin deposition did not occur in the tubular epithelium of control and low dose males and females sacrificed at the end of dosing. This change did occur in 1 out of 10 and 5 out of 5 males, and in 2 out of 10 and 10 out of 10 females in the middle and high dose groups, respectively, sacrificed at this time. Mean group severity scores were 0.10 and 2.20 in males, and 0.20 and 2.20 in females in the middle and high dose groups, respectively. Among animals sacrificed at the end of the recovery period, this change occurred in 0 out of 10 and 2 out of 10 males, and in 0 out of 10 and 1 out of 9 females in the control and high dose groups, respectively. Mean group severity scores for this change were 0.00 and 0.20 in males, and 0.00 and 0.11 in females in the control and high dose groups, respectively.

Hemoglobin that is removed or released from erythrocytes is normally cleared from the blood by combining with heme-binding proteins which are then removed from the circulation. When heme-binding proteins are overloaded, such as in hemolytic anemia, some unbound hemoglobin will form dimers which can pass through the glomerular filtration system and appear as eosinophilic (i.e. proteinic) droplets in the proximal convoluted tubule. Tubular epithelial cells will resorb and metabolize the hemoglobin dimers, but can be damaged if stromal elements of lysed erythrocytes also pass into the glomerular filtrate.³ The hemosiderin deposited in tubular epithelium is additional evidence of hemoglobin passing into the glomerular filtrate. Changes in the lungs suggested that pulmonary vascular permeability was increased. It is less clear whether these renal changes were associated with normal or increased vascular permeability in the glomerulus. For these reasons, and due to incidence and mean group severity scores at the end of dosing and after the recovery period, hemoglobin nephrosis and hemosiderin deposition in tubular epithelium were interpreted as secondary to increased erythrocyte destruction rather than as direct test article-related effects.

Bone Marrow

Evaluation of sections of bone marrow revealed deposition of hemosiderin in 2 out of 5 males and in 5 out of 10 females in the high dose group sacrificed at the end of dosing. Mean group severity scores for this change were 0.40 in high dose males and 0.50 in high dose females. This change did not occur in control, low, or middle dose animals sacrificed at the end of dosing, or in control and high dose animals sacrificed after the recovery period. Evaluation of femoral bone marrow smears of male and female treated animals sacrificed at the end of dosing revealed no treatment-related effect in the M:E ratio (Appendix 1). Hemosiderin deposition in the bone marrow and kidney suggests increased erythrocyte destruction. Increased erythrocyte destruction must have been mild, however, as evidenced by the absence of a decrease in the M:E ratio at the end of dosing. For these reasons, hemosiderin deposition in the bone marrow was interpreted as secondary to mildly increased erythrocyte destruction.

Spleen

Among animals sacrificed at the end of dosing, splenic hyperplasia was diagnosed in 0 out of 10, 4 out of 10, and 5 out of 5 males, and in 0 out of 10, 0 out of 10, and 8 out of 10 females in the low, middle, and high dose groups, respectively. Mean group severity scores for this finding in these animals were 0.00, 0.60, and 2.20 in males, and 0.00, 0.00, and 1.50 in females in the low, middle, and high dose groups, respectively. This change did not occur in control animal sacrificed at the end of dosing or in control and high dose animals sacrificed after the recovery period. The mechanism by which splenic hyperplasia occurred is not clear. Antigenic stimulation of splenic lymphocytes, generalized stimulation of sinusoidal phagocytes, or both seem most likely, as this change was not associated with increased hemosiderin deposits or extramedullary hematopoiesis.

³ N.F. Cheville, Cell Pathology, (Ames: The Iowa State University Press, 1983), p. 578.

Based on dosed-related incidence and mean group severity scores in animals sacrificed at the end of dosing, and on resolution of this change in recovery animals, splenic hyperplasia was interpreted as a direct test article-related effect.

Other Lesions

All other lesions seen were interpreted to be incidental changes and not related to the test article.

In summary, the principal pathology findings in this study were those in the lungs, kidney, bone marrow and spleen. Alveolar proteinosis in the lung was a direct test article-related change in middle and high dose groups. While this change was morphologically distinct, the mechanism of its development was less clear. The two most likely mechanisms would be alteration of the vascular permeability, causing persistent alveolar edema, or alteration of surfactant production and degradation. Chronic inflammation and hemosiderin deposition in alveolar macrophages were considered secondary effects of the test article, representing resolution of alveolar proteinosis. Changes in the kidney and bone marrow were considered secondary to increased erythrocyte destruction. These changes had resolved or were resolving at the end of the recovery period. Splenic hyperplasia was associated with proportional increases in the size of lymphoid and sinusoidal elements rather than with extramedullary hematopoiesis or hemosiderin deposition. Based on incidence and mean group severity scores, splenic hyperplasia was interpreted as a direct test article-related effect in middle and high dose groups at the end of dosing, but the mechanism of its occurrence was not clear.

CONCLUSIONS

Under the conditions of this study, oral administration of WR238605 to rats for thirteen weeks was associated with changes in the lungs, kidneys, bone marrow, and spleen. Alveolar proteinosis was a direct test article-related change in the lungs of middle and high dose animals sacrificed at the end of dosing. Chronic inflammation and hemosiderin deposition in alveolar macrophages occurred in lungs of middle and high dose animals sacrificed after the recovery period. These changes were interpreted as part of the resolution of alveolar proteinosis and were, thus, considered to be secondarily related to the test article.

Hemoglobin nephrosis and hemosiderin deposition occurred in the kidneys of middle and high dose animals at the end of dosing, but were resolving or had resolved by the end of the recovery period. Hemosiderin deposition also occurred in the bone marrow of high dose animals sacrificed at the end of dosing, but had resolved after the recovery period. These changes in kidney and bone marrow were interpreted as secondary to mildly increased erythrocyte destruction, and were considered secondary test article-related effects. This was consistent with the results of bone marrow smear evaluations.

Splenic hyperplasia in the middle and high dose groups was interpreted as a direct test article-related effect, but no mechanism for its occurrence was identified.

The no-effect level was clearly the low dose level (0.5 mg base/kg/day) for direct and secondary test article-related effects. All of the changes observed at the higher doses had resolved or were resolving by the end of the recovery period.

Michael J. Tomlinson, DVM, Ph.D.
Diplomate, ACVP

Date

TABLE I

SUMMARY OF EXPERIMENTAL DESIGN

| Treatment Group | Dose Level (mg base/kg/day) | Number of Males | Number of Females |
|-----------------|--------------------------------|--------------------|----------------------|
| 1 | 0 | 10+10* | 10+10* |
| 2 | 0.5 | 10+10* | 10+10* |
| 3 | 6.0 | 10+10* | 10+10* |
| 4 | 18.0 | 10+10* | 10+10* |

*Recovery Animals

TABLE II

PROTOCOL-REQUIRED TISSUES

| | |
|----------------------------|---------------------------------|
| Adrenal glands | Pituitary |
| Brain | Prostate |
| Cecum | Rib with costochondral junction |
| Colon | Salivary gland (submaxillary) |
| Diaphragm | Sciatic nerve |
| Duodenum | Skeletal muscle |
| Esophagus | Skin with mammary gland |
| Eyes with harderian glands | Spinal cord (thoracic) |
| Femoral marrow smear | Spleen |
| Heart | Sternum with marrow |
| Gross lesions | Stomach |
| Ileum | Testes with epididymides |
| Jejunum | Thymus |
| Kidneys | Thyroid gland with parathyroids |
| Liver | Tongue |
| Lungs/Bronchi | Trachea |
| Lymph node (mesenteric) | Urinary bladder |
| Ovaries | Uterus |
| Pancreas | |

TABLE III
TISSUE ACCOUNTABILITY RECORD

| TREATMENT GROUP | ANIMAL NUMBER | FATE | TISSUE | REASON TISSUE NOT PRESENT |
|-----------------|---------------|------|------------------------|---------------------------|
| 1 | 0803 | TS | Mammary gland | U |
| 1 | 0817 | TS | Parathyroid gland | U |
| 1 | 0821 | TS | Mammary gland | U |
| 1-R | 0835 | TS | Pituitary gland | E |
| 1 | 0839 | TS | Parathyroid gland | U |
| 2 | 0849 | TS | Pituitary gland | E |
| 4 | 0924 | TS | Diaphragm | M |
| 4 | 0925 | TS | Costochondral junction | U |
| 4 | 0926 | ND | Duodenum | A |
| 4 | 0926 | ND | Eyes | A |
| 4 | 0926 | ND | Mammary gland | U |
| 4 | 0934 | ND | Salivary gland | M |
| 4 | 0934 | ND | Parathyroid gland | U |
| 4 | 0934 | ND | Mesenteric lymph node | M |
| 4 | 0936 | ND | Pituitary gland | M |
| 4 | 0936 | ND | Trachea | A |
| 4 | 0936 | ND | Thyroid gland | A |
| 4 | 0936 | ND | Colon | A |
| 4 | 0936 | ND | Ileum | A |
| 4 | 0936 | ND | Cecum | A |
| 4 | 0936 | ND | Mesenteric lymph node | M |
| 4 | 0936 | ND | Eyes | A |
| 4 | 0937 | ND | Thymus | U |
| 4 | 0937 | ND | Parathyroid gland | U |
| 4 | 0938 | TS | Parathyroid gland | U |
| 4-R | 0956 | ND | Parathyroid gland | U |
| 4-R | 0956 | ND | Mammary gland | U |
| 4-R | 0956 | ND | Sciatic nerve | U |

TS: Terminal Sacrifice
ND: Natural Death
U: Unavailable/Unsuitable for microscopic evaluation
M: Not present in wet tissue at trimming
E: Not present in cassette at embedding
A: Autolysis precludes evaluation

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Report Codes Table

A. Codes applying to organs

| | |
|---|--|
| N | Tissues within normal histological limits |
| A | Autolysis precluding adequate evaluation |
| P | Paired organ missing |
| U | Tissues unsuitable for complete evaluation |
| S | Tissues not applicable to animal |
| * | Tissues not required by protocol |

DRAFT

B. Codes applying to microscopic diagnoses

| | |
|---|--|
| 1 | minimal |
| 2 | mild |
| 3 | moderate |
| 4 | marked |
|) | focal |
|] | locally extensive |
| > | multifocal |
| P | Present |
| B | Neoplasm, benign |
| M | Neoplasm, malignant without metastasis |
| C | Neoplasm, malignant with metastasis |
| X | Metastatic site (+) |
| - | No data entered |

HISTOPATHOLOGY TABLES

ABBREVIATION LIST

Cytopl - Cytoplasm
Epith - Epithelium
Granulomat - Granulomatous
Hyperpl - Hyperplasia
Infiltr - Infiltrate
Inflam - Inflammation
Perivasc - Perivascular
R - Recovery
Regenerat - Regeneration
Seminif - Seminiferous
Tubulr - Tubular
Vacuo - Vacuolation

SECTION II
PROJECT SUMMARY TABLE

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
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Project Summary Table

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: MALE

DRAFT

PAGE 15

| | | | | | | | | |
|--------------------|----|----|----|---|-------|-------|-------|-------|
| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 5 | 10 | 10 | 10 | 10 |

| | | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
|---------------------------------|------|----|------|----|-------|----|-------|---|-------|----|-------|---|---|---|------|
| BRAIN | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| PITUITARY GLAND | # Ex | 10 | | 9 | | 10 | | 5 | | 10 | | 0 | | 0 | |
| Pars distalis, cyst | | 1 | (10) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | | 0 | (0) |
| Pars distalis, hyperplasia | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | | 0 | (10) |
| Pars distalis, vacuo, cytopl | | 9 | (90) | 9 | (100) | 10 | (100) | 5 | (100) | 10 | (100) | 0 | | 0 | (90) |
| Pars intermedia, cyst | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) | 0 | | 0 | (0) |
| Rathke's cleft, tubular hyperpl | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | | 0 | (10) |
| SPINAL CORD, THORACIC | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| THYMUS | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| Congestion | | 2 | (20) | 0 | | 0 | | 0 | (0) | 0 | | 0 | | 0 | |
| SALIVARY GLAND | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| PANCREAS | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| Inflammation, chronic | | 1 | (10) | 0 | | 0 | | 0 | (0) | 0 | | 0 | | 0 | |
| Lobule, degeneration | | 0 | (0) | 0 | | 0 | | 1 | (20) | 0 | | 0 | | 0 | |
| ADRENAL GLAND | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| Cortex, vacuolation, cytoplasm | | 6 | (60) | 0 | | 0 | | 2 | (40) | 0 | | 0 | | 0 | |
| TRACHEA | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| THYROID GLAND | # Ex | 10 | | 10 | | 10 | | 5 | | 10 | | 0 | | 0 | |
| PARATHYROID GLAND | # Ex | 9 | | 0 | | 0 | | 4 | | 0 | | 0 | | 0 | |
| ESOPHAGUS | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
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Project Summary Table

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: MALE

DRAFT

PAGE 16

| GROUP: | | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
|-------------------------------|------|--------|----|--------|---|----------|-------|---------|-------|
| NUMBER OF ANIMALS: | | 10 | 10 | 10 | 5 | 10 | 10 | 10 | 10 |
| | | # | % | # | % | # | % | # | % |
| HEART | # Ex | 10 | | 0 | | 5 | | 0 | |
| Cardiomyopathy | | 4 (40) | | 0 | | 1 (20) | | 0 | |
| DUODENUM | # Ex | 10 | | 0 | | 5 | | 0 | |
| COLON | # Ex | 10 | | 0 | | 5 | | 0 | |
| STOMACH | # Ex | 10 | | 0 | | 5 | | 0 | |
| LIVER | # Ex | 10 | | 10 | | 5 | | 10 | |
| Hepatocyte, vacuo, cytoplasm | | 1 (10) | | 3 (30) | | 0 (0) | | 0 (0) | |
| Inflammation, subacute | | 2 (20) | | 0 (0) | | 0 (0) | | 0 (0) | |
| Lobular hyperplasia | | 0 (0) | | 0 (0) | | 0 (0) | | 1 (10) | |
| Periportal, infiltr, cellular | | 0 (0) | | 0 (0) | | 0 (0) | | 1 (10) | |
| Pigment, hemosiderin | | 0 (0) | | 0 (0) | | 1 (20) | | 0 (0) | |
| SPLEEN | # Ex | 10 | | 10 | | 5 | | 10 | |
| Hyperplasia | | 0 (0) | | 0 (0) | | 4 (40) | | 5 (100) | |
| Pigment, hemosiderin | | 0 (0) | | 0 (0) | | 0 (0) | | 0 (0) | |
| JEJUNUM | # Ex | 10 | | 0 | | 5 | | 0 | |
| LUNG | # Ex | 10 | | 10 | | 5 | | 10 | |
| Alveolar epithelium, hyperpl | | 0 (0) | | 0 (0) | | 0 (0) | | 0 (0) | |
| Alveolar hystiocytosis | | 1 (10) | | 0 (0) | | 0 (0) | | 0 (0) | |
| Alveolar proteinosis | | 0 (0) | | 0 (0) | | 10 (100) | | 5 (100) | |
| Hemorrhage | | 2 (20) | | 0 (0) | | 0 (0) | | 2 (20) | |
| Inflammation, chronic | | 0 (0) | | 0 (0) | | 0 (0) | | 0 (0) | |
| Inflammation, perivasc, acute | | 1 (10) | | 0 (0) | | 0 (0) | | 0 (0) | |
| Inflammation, subacute | | 4 (40) | | 0 (0) | | 3 (30) | | 0 (0) | |
| Pigment, hemosiderin | | 1 (10) | | 0 (0) | | 0 (0) | | 1 (10) | |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Project Summary Table

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PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: MALE

D R A F T

PAGE 17

| | | | | | | | | |
|--------------------|----|----|----|---|-------|-------|-------|-------|
| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 5 | 10 | 10 | 10 | 10 |

| | | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
|--------------------------------|------|----|------|----|-----|----|------|---|-------|----|------|---|---|---|------|
| KIDNEY | # Ex | 10 | | 10 | | 10 | | 5 | | 10 | | 0 | | 0 | |
| Cortex, cyst | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) | 0 | | 0 | (0) |
| Infiltrate, cellular | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | | 0 | (10) |
| Nephropathy | | 4 | (40) | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (20) | 0 | | 0 | (10) |
| Nephrosis, hemoglobin | | 0 | (0) | 0 | (0) | 5 | (50) | 5 | (100) | 0 | (0) | 0 | | 0 | (0) |
| Pigment, hemosiderin | | 0 | (0) | 0 | (0) | 1 | (10) | 5 | (100) | 0 | (0) | 0 | | 0 | (20) |
| Renal tubule, dilatation | | 1 | (10) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | | 0 | (0) |
| Renal tubule, epith, regenerat | | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) | 1 | (10) | 0 | | 0 | (0) |
| URINARY BLADDER | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| Calculus | | 3 | (30) | 0 | | 0 | | 1 | (20) | 0 | | 0 | | 0 | |
| Epithelium, ulcer | | 1 | (10) | 0 | | 0 | | 0 | (0) | 0 | | 0 | | 0 | |
| PROSTATE | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| Inflammation, subacute | | 1 | (10) | 0 | | 0 | | 0 | (0) | 0 | | 0 | | 0 | |
| SKIN | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| MAMMARY GLAND | # Ex | 9 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| ILEUM | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| CECUM | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| LYMPH NODE, MESENTERIC | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| SKELETAL MUSCLE | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |
| SCIATIC NERVE | # Ex | 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Project Summary Table

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098

WEEKS: 14-27

FATES: Terminal Sacrifice

SEX: MALE

DRAFT

PAGE 18

| | | | | | | | | |
|--------------------|----|----|----|---|-------|-------|-------|-------|
| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 5 | 10 | 10 | 10 | 10 |

| | # | % | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
|------------------------------|---------|-----|----|-----|----|-----|---|------|----|-----|---|---|---|---|----|-----|
| TESTES | # Ex 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | | 0 | |
| Seminif tubules, giant cells | 0 | (0) | 0 | | 0 | | 1 | (20) | 0 | | 0 | | 0 | | 0 | |
| EPIDIDYMIS | # Ex 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | | 0 | |
| TONGUE | # Ex 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | | 0 | |
| DIAPHRAGM | # Ex 10 | | 0 | | 0 | | 4 | | 0 | | 0 | | 0 | | 0 | |
| RIB | # Ex 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | | 0 | |
| COSTOCHONDRAL JUNCTION | # Ex 10 | | 0 | | 0 | | 4 | | 0 | | 0 | | 0 | | 0 | |
| STERNUM | # Ex 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | | 0 | |
| BONE MARROW | # Ex 10 | | 10 | | 10 | | 5 | | 10 | | 0 | | 0 | | 10 | |
| Pigment, hemosiderin | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (40) | 0 | (0) | 0 | | 0 | | 0 | (0) |
| EYE | # Ex 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | | 0 | |
| HARDERIAN GLAND | # Ex 10 | | 0 | | 0 | | 5 | | 0 | | 0 | | 0 | | 0 | |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
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PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: FEMALE

DRAFT

PAGE 19

| | | | | | | | | |
|--------------------|----|----|----|----|-------|-------|-------|-------|
| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |

| | # | % | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
|------------------------------|------|----|------|---|----|-----|----|-----|----|------|----|------|---|---|---|-----|
| BRAIN | # Ex | 10 | | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| PITUITARY GLAND | # Ex | 10 | | | 10 | | 10 | | 9 | | 0 | | 0 | | 9 | |
| Pars distalis, adenoma | | 0 | (0) | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (22) | 0 | | 0 | (0) |
| Pars distalis, cyst | | 1 | (10) | | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) | 0 | | 0 | (0) |
| Pars distalis, vacuo, cytopl | | 0 | (0) | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (22) | 0 | | 0 | (0) |
| Pars intermedia, cyst | | 0 | (0) | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (11) | 0 | | 0 | (0) |
| SPINAL CORD, THORACIC | # Ex | 10 | | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| THYMUS | # Ex | 10 | | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| SALIVARY GLAND | # Ex | 10 | | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| PANCREAS | # Ex | 10 | | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| ADRENAL GLAND | # Ex | 10 | | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| Cortex, cystic degeneration | | 1 | (10) | | 0 | | 0 | | 0 | (0) | 0 | | 0 | | 0 | |
| Cortex, pigment, lipofuscin | | 0 | (0) | | 0 | | 0 | | 2 | (20) | 0 | | 0 | | 0 | |
| TRACHEA | # Ex | 10 | | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| THYROID GLAND | # Ex | 10 | | | 10 | | 10 | | 10 | | 10 | | 0 | | 0 | |
| PARATHYROID GLAND | # Ex | 9 | | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| Fibrosis | | 1 | (11) | | 0 | | 0 | | 0 | (0) | 0 | | 0 | | 0 | |
| ESOPHAGUS | # Ex | 10 | | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Project Summary Table

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

DRAFT

PAGE 20

PROJECT ID. NO: TRL098

FATES: Terminal Sacrifice

WEEKS: 14-27

SEX: FEMALE

| GROUP: | | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
|-------------------------------|------|----|------|----|------|-------|-------|-------|-------|
| NUMBER OF ANIMALS: | | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |
| | | # | % | # | % | # | % | # | % |
| HEART | # Ex | 10 | | 0 | | 0 | | 0 | |
| Cardiomyopathy | | 0 | (0) | 0 | | 2 | (20) | 0 | |
| Hemorrhage | | 1 | (10) | 0 | | 0 | (0) | 0 | |
| DUODENUM | # Ex | 10 | | 0 | | 0 | | 0 | |
| COLON | # Ex | 10 | | 0 | | 0 | | 0 | |
| STOMACH | # Ex | 10 | | 0 | | 0 | | 0 | |
| Non-glandular, inflammation | | 1 | (10) | 0 | | 0 | (0) | 0 | |
| LIVER | # Ex | 10 | | 10 | | 10 | | 0 | |
| Basophilic focus | | 0 | (0) | 1 | (10) | 0 | (0) | 0 | |
| Bile duct, hyperplasia | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | |
| Hepatocyte, vacuo, cytoplasm | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) |
| Infiltrate, cellular | | 0 | (0) | 0 | (0) | 3 | (30) | 0 | |
| Inflammation, subacute | | 3 | (30) | 0 | (0) | 0 | (0) | 0 | |
| Periportal, infiltr, cellular | | 0 | (0) | 1 | (10) | 0 | (0) | 0 | |
| Pigment, hemosiderin | | 0 | (0) | 0 | (0) | 2 | (20) | 0 | |
| Portal, fibrosis | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | |
| SPLEEN | # Ex | 10 | | 10 | | 10 | | 0 | |
| Hyperplasia | | 0 | (0) | 0 | (0) | 8 | (80) | 0 | |
| Pigment, hemosiderin | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | |
| JEJUNUM | # Ex | 10 | | 0 | | 0 | | 0 | |
| LUNG | # Ex | 10 | | 10 | | 10 | | 10 | |
| Alveolar hystiocytosis | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) |
| Alveolar proteinosis | | 0 | (0) | 0 | (0) | 10 | (100) | 0 | (0) |
| Hemorrhage | | 1 | (10) | 0 | (0) | 0 | (0) | 1 | (10) |
| Inflammation, acute | | 0 | (0) | 0 | (0) | 2 | (20) | 0 | (0) |
| Inflammation, chronic | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) |
| Inflammation, subacute | | 2 | (20) | 0 | (0) | 5 | (50) | 1 | (10) |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
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PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: FEMALE

D R A F T

PAGE 21

| | | | | | | | | |
|--------------------|----|----|----|----|-------|-------|-------|-------|
| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |

| | | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
|--------------------------------|------|----|------|----|------|----|------|----|-------|----|------|----|-----|---|------|
| LUNG | # Ex | 10 | | 10 | | 10 | | 10 | | 10 | | 10 | | 9 | |
| Pigment, hemosiderin | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 8 | (80) |
| KIDNEY | # Ex | 10 | | 10 | | 10 | | 10 | | 10 | | 0 | | 9 | |
| Cortex, cyst | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | | 1 | (11) |
| Nephrocalcinosis | | 7 | (70) | 6 | (60) | 5 | (50) | 4 | (40) | 6 | (60) | 0 | | 7 | (78) |
| Nephropathy | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | | 1 | (11) |
| Nephrosis, hemoglobin | | 0 | (0) | 0 | (0) | 4 | (40) | 10 | (100) | 0 | (0) | 0 | | 0 | (0) |
| Pigment, hemosiderin | | 0 | (0) | 0 | (0) | 2 | (20) | 10 | (100) | 0 | (0) | 0 | | 1 | (11) |
| Renal tubule, casts, proteinic | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) | 0 | | 0 | (0) |
| URINARY BLADDER | # Ex | 10 | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| SKIN | # Ex | 10 | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| MAMMARY GLAND | # Ex | 9 | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| ILEUM | # Ex | 10 | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| CECUM | # Ex | 10 | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| LYMPH NODE, MESENTERIC | # Ex | 10 | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| SKELETAL MUSCLE | # Ex | 10 | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| SCIATIC NERVE | # Ex | 10 | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |
| OVARY | # Ex | 10 | | 0 | | 0 | | 10 | | 0 | | 0 | | 0 | |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
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PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: FEMALE

D R A F T

PAGE 22

| | | | | | | | | |
|--------------------|----|----|----|----|-------|-------|-------|-------|
| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |

| | # | % | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
|------------------------|------|----|------|----|-----|----|-----|------|------|---|-----|---|---|---|---|-----|
| UTERUS | # Ex | 10 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Decidua | | 1 | (10) | 0 | 0 | 0 | 0 | (0) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Dilatation | | 3 | (30) | 0 | 0 | 0 | 3 | (30) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Hemorrhage | | 1 | (10) | 0 | 0 | 0 | 0 | (0) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Inflammation, acute | | 1 | (10) | 0 | 0 | 0 | 0 | (0) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | | |
| TONGUE | # Ex | 10 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | | |
| DIAPHRAGM | # Ex | 10 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | | |
| RIB | # Ex | 10 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | | |
| COSTOCHONDRAL JUNCTION | # Ex | 10 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | | |
| STERNUM | # Ex | 10 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | | |
| BONE MARROW | # Ex | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 9 | 9 | 9 |
| Pigment, hemosiderin | | 0 | (0) | 0 | (0) | 0 | (0) | 5 | (50) | 0 | (0) | 0 | 0 | 0 | 0 | (0) |
| | | | | | | | | | | | | | | | | |
| EYE | # Ex | 10 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | | |
| HARDERIAN GLAND | # Ex | 10 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Infiltrate, cellular | | 0 | (0) | 0 | 0 | 0 | 1 | (10) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Inflammation, subacute | | 1 | (10) | 0 | 0 | 0 | 0 | (0) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Project Summary Table

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

PROJECT ID. NO: TRL098

WEEKS: 14-27

FATES: Terminal Sacrifice

SEX: FEMALE

D R A F T

PAGE 23

| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
|--------------------|----|----|----|----|-------|-------|-------|-------|
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |

OTHER TISSUES AND LESIONS:

| | # | % | # | % | # | % | # | % | # | % | # | % | # | % |
|--------------------------------|---|------|---|-----|---|-----|---|------|---|-----|---|-----|---|-----|
| SKIN, EAR - Inflam, granulomat | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) | 0 | (0) | 0 | (0) |
| SKIN - Granuloma, foreign body | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (10) | 0 | (0) | 0 | (0) | 0 | (0) |
| SKIN, HEAD - Inflam, chronic | 1 | (10) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) |

09-Sep-1993

SECTION III
SEVERITY SUMMARY TABLE

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

| | | | | | | | | | | | |
|--------------------------------|------|---------------------------|-------|-------|-------|-------|-------|-------|-------|---------|------|
| PROJECT ID. NO: TRL098 | | FATES: Terminal Sacrifice | | | | DRAFT | | | | PAGE 25 | |
| WEEKS: 14-27 | | SEX: MALE | | | | | | | | | |
| GROUP: | | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R | | |
| NUMBER OF ANIMALS: | | 10 | 10 | 10 | 5 | 10 | 10 | 10 | 10 | | |
| <hr/> | | | | | | | | | | | |
| BRAIN | # Ex | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | |
| | 10 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | |
| PITUITARY GLAND | # Ex | 10 | 9 | 10 | 5 | 10 | 0 | 0 | 0 | 10 | |
| Pars distalis, hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.10 |
| Pars distalis, vacuo, cytopl | | 9 | 0.90 | 9 | 1.11 | 10 | 1.50 | 5 | 1.40 | 10 | 1.30 |
| Rathke's cleft, tubulr hyperpl | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Rathke's cleft, tubulr hyperpl | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0.10 |
| SPINAL CORD, THORACIC | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | |
| THYMUS | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | |
| Congestion | | 2 | 0.30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| SALIVARY GLAND | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | |
| PANCREAS | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | |
| Inflammation, chronic | | 1 | 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| Lobule, degeneration | | 0 | 0 | 0 | 1 | 0.20 | 0 | 0 | 0 | 0 | |
| ADRENAL GLAND | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | |
| Cortex, vacuolation, cytoplasm | | 6 | 0.70 | 0 | 0 | 2 | 0.40 | 0 | 0 | 0 | |
| TRACHEA | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | |
| THYROID GLAND | # Ex | 10 | 10 | 10 | 5 | 10 | 0 | 0 | 0 | 10 | |
| PARATHYROID GLAND | # Ex | 9 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | |
| ESOPHAGUS | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 | 0 | |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

DRAFT

PAGE 26

PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: MALE

| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
|-------------------------------|---------|--------|---------|--------|--------|--------|--------|--------|
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 5 | 10 | 10 | 10 | 10 |
| | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV |
| HEART | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| Cardiomyopathy | 4 0.40 | 0 | 0 | 1 0.20 | 0 | 0 | 0 | 0 |
| DUODENUM | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| COLON | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| STOMACH | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| LIVER | # Ex 10 | 10 | 10 | 5 | 10 | 0 | 0 | 10 |
| Hepatocyte, vacuo, cytoplasm | 1 0.10 | 3 0.40 | 0 | 0 | 0 | 0 | 0 | 1 0.10 |
| Inflammation, subacute | 2 0.20 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lobular hyperplasia | 0 | 0 | 0 | 0 | 1 0.20 | 0 | 0 | 0 |
| Periportal, infiltr, cellular | 0 | 0 | 0 | 0 | 1 0.10 | 0 | 0 | 0 |
| Pigment, hemosiderin | 0 | 0 | 0 | 1 0.20 | 0 | 0 | 0 | 0 |
| SPLEEN | # Ex 10 | 10 | 10 | 5 | 10 | 0 | 0 | 10 |
| Hyperplasia | 0 | 0 | 4 0.60 | 5 2.20 | 0 | 0 | 0 | 0 |
| Pigment, hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 0.10 |
| JEJUNUM | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| LUNG | # Ex 10 | 10 | 10 | 5 | 10 | 10 | 10 | 10 |
| Alveolar epithelium, hyperpl | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 0.10 |
| Alveolar hystiocytosis | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 3 0.30 |
| Alveolar proteinosis | 0 | 0 | 10 1.70 | 5 2.80 | 0 | 0 | 0 | 0 |
| Hemorrhage | 2 0.30 | 0 | 0 | 0 | 2 0.20 | 4 0.40 | 2 0.20 | 0 |
| Inflammation, chronic | 0 | 0 | 0 | 0 | 0 | 0 | 5 0.50 | 1 0.20 |
| Inflammation, perivasc, acute | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Inflammation, subacute | 4 0.60 | 0 | 3 0.30 | 0 | 2 0.20 | 3 0.30 | 3 0.30 | 2 0.20 |
| Pigment, hemosiderin | 1 0.20 | 0 | 0 | 0 | 0 | 1 0.10 | 7 0.80 | 8 0.80 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

D R A F T

PAGE 27

PROJECT ID. NO: TRL098

WEEKS: 14-27

FATES: Terminal Sacrifice

SEX: MALE

| GROUP: | | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
|--------------------------------|------|--------|-------|--------|--------|--------|-------|-------|--------|
| NUMBER OF ANIMALS: | | 10 | 10 | 10 | 5 | 10 | 10 | 10 | 10 |
| | | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV |
| KIDNEY | # Ex | 10 | 10 | 10 | 5 | 10 | 0 | 0 | 10 |
| Infiltrate, cellular | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 0.10 |
| Nephropathy | | 4 0.40 | 0 | 0 | 0 | 2 0.20 | 0 | 0 | 1 0.10 |
| Nephrosis, hemoglobin | | 0 | 0 | 5 0.50 | 5 2.20 | 0 | 0 | 0 | 0 |
| Pigment, hemosiderin | | 0 | 0 | 1 0.10 | 5 2.20 | 0 | 0 | 0 | 2 0.20 |
| Renal tubule, dilatation | | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Renal tubule, epith, regenerat | | 0 | 0 | 1 0.10 | 0 | 1 0.10 | 0 | 0 | 0 |
| URINARY BLADDER | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| Epithelium, ulcer | | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROSTATE | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| Inflammation, subacute | | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SKIN | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| MAMMARY GLAND | # Ex | 9 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| ILEUM | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| CECUM | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| LYMPH NODE, MESENTERIC | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| SKELETAL MUSCLE | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| SCIATIC NERVE | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| TESTES | # Ex | 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| Seminif tubules, giant cells | | 0 | 0 | 0 | 1 0.20 | 0 | 0 | 0 | 0 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: MALE

D R A F T

PAGE 28

| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
|------------------------|---------|-------|-------|--------|-------|-------|-------|-------|
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 5 | 10 | 10 | 10 | 10 |
| | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV |
| EPIDIDYMIS | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| TONGUE | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| DIAPHRAGM | # Ex 10 | 0 | 0 | 4 | 0 | 0 | 0 | 0 |
| RIB | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| COSTOCHONDRAL JUNCTION | # Ex 10 | 0 | 0 | 4 | 0 | 0 | 0 | 0 |
| STERNUM | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| BONE MARROW | # Ex 10 | 10 | 10 | 5 | 10 | 0 | 0 | 10 |
| Pigment, hemosiderin | 0 | 0 | 0 | 2 0.40 | 0 | 0 | 0 | 0 |
| EYE | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |
| HARDERIAN GLAND | # Ex 10 | 0 | 0 | 5 | 0 | 0 | 0 | 0 |

* Severity calculated by the number of tissues examined.

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: FEMALE

DRAFT

PAGE 29

| GROUP: | | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
|------------------------------|------|--------|-------|-------|--------|--------|-------|-------|-------|
| NUMBER OF ANIMALS: | | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |
| | | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV |
| BRAIN | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| PITUITARY GLAND | # Ex | 10 | 10 | 10 | 10 | 9 | 0 | 0 | 9 |
| Pars distalis, vacuo, cytopl | | 0 | 0 | 0 | 0 | 2 0.22 | 0 | 0 | 0 |
| SPINAL CORD, THORACIC | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| THYMUS | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| SALIVARY GLAND | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| PANCREAS | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| ADRENAL GLAND | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| Cortex, cystic degeneration | | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Cortex, pigment, lipofuscin | | 0 | 0 | 0 | 2 0.20 | 0 | 0 | 0 | 0 |
| TRACHEA | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| THYROID GLAND | # Ex | 10 | 10 | 10 | 10 | 10 | 0 | 0 | 9 |
| PARATHYROID GLAND | # Ex | 9 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| Fibrosis | | 1 0.22 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ESOPHAGUS | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| HEART | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| Cardiomyopathy | | 0 | 0 | 0 | 2 0.20 | 0 | 0 | 0 | 0 |
| Hemorrhage | | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

| | | | | | | | | | |
|-------------------------------|------|---------------------------|--------|---------|---------|--------|--------|---------|--------|
| PROJECT ID. NO: TRL098 | | FATES: Terminal Sacrifice | | | | DRAFT | | PAGE 30 | |
| WEEKS: 14-27 | | SEX: FEMALE | | | | | | | |
| GROUP: | | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
| NUMBER OF ANIMALS: | | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |
| <hr/> | | | | | | | | | |
| | | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV |
| DUODENUM | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| COLON | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| STOMACH | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| Non-glandular, inflammation | | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LIVER | # Ex | 10 | 10 | 10 | 10 | 10 | 0 | 0 | 9 |
| Basophilic focus | | 0 | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 |
| Bile duct, hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 0.67 |
| Hepatocyte, vacuo, cytoplasm | | 0 | 0 | 0 | 0 | 1 0.10 | 0 | 0 | 0 |
| Infiltrate, cellular | | 0 | 0 | 3 0.30 | 0 | 0 | 0 | 0 | 0 |
| Inflammation, subacute | | 3 0.30 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Periportal, infiltr, cellular | | 0 | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 1 0.11 |
| Pigment, hemosiderin | | 0 | 0 | 2 0.20 | 0 | 0 | 0 | 0 | 0 |
| Portal, fibrosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 0.11 |
| SPLEEN | # Ex | 10 | 10 | 10 | 10 | 10 | 0 | 0 | 9 |
| Hyperplasia | | 0 | 0 | 0 | 8 1.50 | 0 | 0 | 0 | 0 |
| Pigment, hemosiderin | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 0.11 |
| JEJUNUM | # Ex | 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| LUNG | # Ex | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |
| Alveolar hystiocytosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 0.33 |
| Alveolar proteinosis | | 0 | 0 | 10 1.60 | 10 2.20 | 0 | 0 | 0 | 0 |
| Hemorrhage | | 1 0.10 | 0 | 0 | 0 | 0 | 1 0.10 | 0 | 0 |
| Inflammation, acute | | 0 | 0 | 0 | 2 0.20 | 0 | 0 | 0 | 0 |
| Inflammation, chronic | | 0 | 0 | 0 | 0 | 0 | 0 | 7 1.10 | 5 0.67 |
| Inflammation, subacute | | 2 0.20 | 0 | 5 0.50 | 1 0.10 | 0 | 0 | 1 0.10 | 0 |
| Pigment, hemosiderin | | 0 | 0 | 0 | 0 | 0 | 0 | 8 1.20 | 9 1.11 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: FEMALE

DRAFT

PAGE 31

| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
|--------------------------------|---------|--------|--------|---------|--------|-------|-------|--------|
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |
| | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV | # SEV |
| KIDNEY | # Ex 10 | 10 | 10 | 10 | 10 | 0 | 0 | 9 |
| Nephrocalcinosis | 7 0.90 | 6 0.60 | 5 0.50 | 4 0.40 | 6 0.60 | 0 | 0 | 7 0.89 |
| Nephropathy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 0.11 |
| Nephrosis, hemoglobin | 0 | 0 | 4 0.40 | 10 1.50 | 0 | 0 | 0 | 0 |
| Pigment, hemosiderin | 0 | 0 | 2 0.20 | 10 2.20 | 0 | 0 | 0 | 1 0.11 |
| Renal tubule, casts, proteinic | 0 | 0 | 0 | 0 | 1 0.10 | 0 | 0 | 0 |
| URINARY BLADDER | # Ex 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| SKIN | # Ex 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| MAMMARY GLAND | # Ex 9 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| ILEUM | # Ex 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| CECUM | # Ex 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| LYMPH NODE, MESENTERIC | # Ex 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| SKELETAL MUSCLE | # Ex 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| SCIATIC NERVE | # Ex 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| OVARY | # Ex 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| UTERUS | # Ex 10 | 0 | 0 | 10 | 0 | 0 | 0 | 0 |
| Deciduoma | 1 0.20 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Dilatation | 3 0.50 | 0 | 0 | 3 0.60 | 0 | 0 | 0 | 0 |
| Hemorrhage | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Inflammation, acute | 1 0.10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Severity Summary Table

DRAFT

PAGE 32

PROJECT ID. NO: TRL098
WEEKS: 14-27

FATES: Terminal Sacrifice
SEX: FEMALE

| | | | | | | | | |
|--------------------|----|----|----|----|-------|-------|-------|-------|
| GROUP: | 1 | 2 | 3 | 4 | 1 - R | 2 - R | 3 - R | 4 - R |
| NUMBER OF ANIMALS: | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 9 |

| | # | Ex | SEV | # | Ex | SEV | # | Ex | SEV | # | Ex | SEV | # | Ex | SEV | # | Ex | SEV | # | Ex | SEV |
|------------------------|---|----|-----|---|----|------|---|----|-----|---|----|-----|---|----|------|---|----|-----|---|----|-----|
| TONGUE | | | 10 | | | 0 | | | 0 | | | 10 | | | 0 | | | 0 | | | 0 |
| DIAPHRAGM | | | 10 | | | 0 | | | 0 | | | 10 | | | 0 | | | 0 | | | 0 |
| RIB | | | 10 | | | 0 | | | 0 | | | 10 | | | 0 | | | 0 | | | 0 |
| COSTOCHONDRAL JUNCTION | | | 10 | | | 0 | | | 0 | | | 10 | | | 0 | | | 0 | | | 0 |
| STERNUM | | | 10 | | | 0 | | | 0 | | | 10 | | | 0 | | | 0 | | | 0 |
| BONE MARROW | | | 10 | | | 10 | | | 10 | | | 10 | | | 10 | | | 0 | | | 9 |
| Pigment, hemosiderin | | | 0 | | | 0 | | | 0 | | | 5 | | | 0.50 | | | 0 | | | 0 |
| EYE | | | 10 | | | 0 | | | 0 | | | 10 | | | 0 | | | 0 | | | 0 |
| HARDERIAN GLAND | | | 10 | | | 0 | | | 0 | | | 10 | | | 0 | | | 0 | | | 0 |
| Infiltrate, cellular | | | 0 | | | 0 | | | 0 | | | 1 | | | 0.10 | | | 0 | | | 0 |
| Inflammation, subacute | | | 1 | | | 0.10 | | | 0 | | | 0 | | | 0 | | | 0 | | | 0 |

* Severity calculated by the number of tissues examined.

09-Sep-1993

SECTION IV
TABULATED ANIMAL DATA

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 34

PROJECT ID: TRL098

GROUP: 1

SEX: MALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0803 | 0804 | 0805 | 0808 | 0812 | 0813 | 0817 | 0818 | 0819 | 0820 |
|--------------------------------|------|------|------|------|------|------|------|------|------|------|
| BRAIN | N | N | N | N | N | N | N | N | N | N |
| PITUITARY GLAND | | N | | | | | | | | |
| Pars distalis, cyst | - | - | - | - | - | - | - | - | - | P |
| Pars distalis, vacuo, cytopl | 1 | - | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| SPINAL CORD, THORACIC | N | N | N | N | N | N | N | N | N | N |
| THYMUS | | | N | N | N | N | N | N | N | N |
| Congestion | 2 | 1 | - | - | - | - | - | - | - | - |
| SALIVARY GLAND | N | N | N | N | N | N | N | N | N | N |
| PANCREAS | N | | N | N | N | N | N | N | N | N |
| Inflammation, chronic | - | 1 | - | - | - | - | - | - | - | - |
| ADRENAL GLAND | N | | | | N | | N | | | N |
| Cortex, vacuolation, cytoplasm | - | 1 | 1 | 1 | - | 1 | - | 2 | 1 | - |
| TRACHEA | N | N | N | N | N | N | N | N | N | N |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| PARATHYROID GLAND | N | N | N | N | N | N | U | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 35

| ANIMAL ID: | 0803 | 0804 | 0805 | 0808 | 0812 | 0813 | 0817 | 0818 | 0819 | 0820 |
|-------------------------------|------|------|------|------|------|------|------|------|------|------|
| ESOPHAGUS | N | N | N | N | N | N | N | N | N | N |
| HEART | N | | N | N | N | | N | | N | |
| Cardiomyopathy | - | 1 | - | - | - | 1 | - | 1 | - | 1 |
| DUODENUM | N | N | N | N | N | N | N | N | N | N |
| COLON | N | N | N | N | N | N | N | N | N | N |
| STOMACH | N | N | N | N | N | N | N | N | N | N |
| LIVER | N | N | N | N | N | N | N | | | N |
| Hepatocyte, vacuo, cytoplasm | - | - | - | - | - | - | - | 1 | - | - |
| Inflammation, subacute | - | - | - | - | - | - | - | 1 | 1 | - |
| SPLEEN | N | N | N | N | N | N | N | N | N | N |
| JEJUNUM | N | N | N | N | N | N | N | N | N | N |
| LUNG | | | | | | N | N | N | | |
| Alveolar hystiocytosis | - | 1 | - | - | - | - | - | - | - | - |
| Hemorrhage | 2 | - | - | - | 1 | - | - | - | - | - |
| Inflammation, perivasc, acute | - | - | 1 | - | - | - | - | - | - | - |
| Inflammation, subacute | 1 | - | - | 2 | - | - | - | - | 1 | 2 |
| Pigment, hemosiderin | 2 | - | - | - | - | - | - | - | - | - |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

DRAFT

PAGE 36

| ANIMAL ID: | 0803 | 0804 | 0805 | 0808 | 0812 | 0813 | 0817 | 0818 | 0819 | 0820 |
|--------------------------|------|------|------|------|------|------|------|------|------|------|
| KIDNEY | | N | | N | | | | N | N | N |
| Nephropathy | 1 | - | - | - | 1 | 1 | 1 | - | - | - |
| Renal tubule, dilatation | - | - | 1 | - | - | - | - | - | - | - |
| URINARY BLADDER | | N | N | | N | N | | | N | N |
| Calculus | P | - | - | P | - | - | P | - | - | - |
| Epithelium, ulcer | - | - | - | - | - | - | - | 1 | - | - |
| PROSTATE | N | N | N | N | | N | N | N | N | N |
| Inflammation, subacute | - | - | - | - | 1 | - | - | - | - | - |
| SKIN | N | N | N | N | N | N | N | N | N | N |
| MAMMARY GLAND | U | N | N | N | N | N | N | N | N | N |
| ILEUM | N | N | N | N | N | N | N | N | N | N |
| CECUM | N | N | N | N | N | N | N | N | N | N |
| LYMPH NODE, MESENTERIC | N | N | N | N | N | N | N | N | N | N |
| SKELETAL MUSCLE | N | N | N | N | N | N | N | N | N | N |
| SCIATIC NERVE | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

DRAFT

PAGE 37

| ANIMAL ID: | 0803 | 0804 | 0805 | 0808 | 0812 | 0813 | 0817 | 0818 | 0819 | 0820 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| TESTES | N | N | N | N | N | N | N | N | N | N |
| EPIDIDYMIS | N | N | N | N | N | N | N | N | N | N |
| TONGUE | N | N | N | N | N | N | N | N | N | N |
| DIAPHRAGM | N | N | N | N | N | N | N | N | N | N |
| RIB | N | N | N | N | N | N | N | N | N | N |
| COSTOCHONDRAL JUNCTION | N | N | N | N | N | N | N | N | N | N |
| STERNUM | N | N | N | N | N | N | N | N | N | N |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |
| EYE | N | N | N | N | N | N | N | N | N | N |
| HARDERIAN GLAND | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

DRAFT

PAGE 38

| ANIMAL ID: | 0841 | 0842 | 0843 | 0845 | 0847 | 0849 | 0854 | 0855 | 0856 | 0857 |
|------------------------------|------|------|------|------|------|------|------|------|------|------|
| PITUITARY GLAND | | | | | | U | | | | |
| Pars distalis, vacuo, cytopl | 2 | 1 | 1 | 1 | 1 | - | 1 | 1 | 1 | 1 |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| LIVER | N | N | | N | N | | | N | N | N |
| Hepatocyte, vacuo, cytoplasm | - | - | 2 | - | - | 1 | 1 | - | - | - |
| SPLEEN | N | N | N | N | N | N | N | N | N | N |
| LUNG | N | N | N | N | N | N | N | N | N | N |
| KIDNEY | N | N | N | N | N | N | N | N | N | N |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 39

PROJECT ID: TRL098

GROUP: 3

SEX: MALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0881 | 0882 | 0883 | 0885 | 0886 | 0888 | 0891 | 0892 | 0894 | 0898 |
|--------------------------------|------|------|------|------|------|------|------|------|------|------|
| PITUITARY GLAND | | | | | | | | | | |
| Pars distalis, vacuo, cytopl | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 1 | 2 |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| LIVER | N | N | N | N | N | N | N | N | N | N |
| SPLEEN | | | N | N | N | | | N | N | N |
| Hyperplasia | 1 | 1 | - | - | - | 2 | 2 | - | - | - |
| LUNG | | | | | | | | | | |
| Alveolar proteinosis | 2 | 2 | 2 | 2 | 1 | 2 | 1 | 1 | 2 | 2 |
| Inflammation, subacute | - | - | 1 | 1 | - | 1 | - | - | - | - |
| KIDNEY | | | | N | N | | | N | N | |
| Nephrosis, hemoglobin | 1 | 1 | 1 | - | - | 1 | - | - | - | 1 |
| Pigment, hemosiderin | - | - | - | - | - | - | - | - | - | 1 |
| Renal tubule, epith, regenerat | - | - | - | - | - | - | 1 | - | - | - |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4
SEX: MALE
FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 40

| ANIMAL ID: | 0921 | 0924 | 0925 | 0926 | 0928 | 0931 | 0934 | 0936 | 0937 | 0938 |
|--------------------------------|------|------|------|------|------|------|------|------|------|------|
| BRAIN | | N | N | N | N | N | N | | N | N |
| Cerebrum, hemorrhage | 1 | - | - | - | - | - | - | 1 | - | - |
| Medulla, hemorrhage | 1 | - | - | - | - | - | - | - | - | - |
| PITUITARY GLAND | | | | N | | | | U | N | |
| Inflammation, acute | 1 | - | - | - | - | - | - | - | - | - |
| Pars distalis, vacuo, cytopl | - | 2 | 1 | - | 2 | 1 | 1 | - | - | 1 |
| SPINAL CORD, THORACIC | N | N | N | N | N | N | N | N | N | N |
| THYMUS | | N | N | N | N | N | N | N | U | N |
| Depletion, lymphocyte | 4 | - | - | - | - | - | - | - | - | - |
| SALIVARY GLAND | N | N | N | N | N | N | U | N | N | N |
| PANCREAS | N | N | N | N | N | | N | N | N | N |
| Lobule, degeneration | - | - | - | - | - | 1 | - | - | - | - |
| ADRENAL GLAND | | | N | N | N | | | N | N | N |
| Cortex, congestion | - | - | - | - | - | - | 1 | - | - | - |
| Cortex, vacuolation, cytoplasm | 1 | 1 | - | - | - | 1 | - | - | - | - |
| TRACHEA | N | N | N | N | N | N | N | A | N | N |
| THYROID GLAND | N | N | N | N | N | N | N | A | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 41

| ANIMAL ID: | 0921 | 0924 | 0925 | 0926 | 0928 | 0931 | 0934 | 0936 | 0937 | 0938 |
|------------------------------|------|------|------|------|------|------|------|------|------|------|
| PARATHYROID GLAND | N | N | N | N | N | N | U | N | U | U |
| ESOPHAGUS | N | N | N | N | N | N | N | N | N | N |
| HEART | | | N | | N | N | N | N | | N |
| Cardiomyopathy | - | 1 | - | - | - | - | - | - | - | - |
| Epicardium, inflam, subacute | 3 | - | - | - | - | - | - | - | 4 | - |
| Inflammation, acute | - | - | - | 1 | - | - | - | - | - | - |
| DUODENUM | N | N | N | A | N | N | N | N | N | N |
| COLON | N | N | N | N | N | N | N | A | N | N |
| STOMACH | N | N | N | N | N | N | N | N | N | N |
| LIVER | N | N | N | | N | | N | N | N | N |
| Pigment, hemosiderin | - | - | - | 1 | - | 1 | - | - | - | - |
| SPLEEN | N | | | N | | | N | N | N | |
| Hyperplasia | - | 2 | 3 | - | 2 | 2 | - | - | - | 2 |
| JEJUNUM | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 42

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

| ANIMAL ID: | 0921 | 0924 | 0925 | 0926 | 0928 | 0931 | 0934 | 0936 | 0937 | 0938 |
|--------------------------------|------|------|------|------|------|------|------|------|------|------|
| LUNG | | | | N | | | | N | | |
| Alveolar proteinosis | - | 3 | 2 | - | 3 | 3 | 3 | - | - | 3 |
| Congestion | 3 | - | - | - | - | - | - | - | - | - |
| Hemorrhage | 2 | - | - | - | - | - | - | - | - | - |
| Inflammation, acute | 2 | - | - | - | - | - | - | - | - | - |
| Microthrombosis | 3 | - | - | - | - | - | - | - | - | - |
| Pleura, inflammation, subacute | 3 | - | - | - | - | - | - | - | 4 | - |
| KIDNEY | N | | | N | | | | N | N | |
| Nephrosis, hemoglobin | - | 3 | 2 | - | 1 | 3 | 2 | - | - | 2 |
| Pigment, hemosiderin | - | 2 | 3 | - | 2 | 2 | 1 | - | - | 2 |
| URINARY BLADDER | N | N | N | N | N | | | | N | N |
| Calculus | - | - | - | - | - | P | P | P | - | - |
| PROSTATE | N | N | N | N | N | N | N | N | N | N |
| SKIN | N | N | N | N | N | N | N | N | N | N |
| MAMMARY GLAND | N | N | N | U | N | N | N | N | N | N |
| ILEUM | N | N | N | N | N | N | N | A | N | N |
| CECUM | N | N | N | N | N | N | N | A | N | N |
| LYMPH NODE, MESENTERIC | N | N | N | N | N | N | U | U | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 43

PROJECT ID: TRL098

GROUP: 4

SEX: MALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0921 | 0924 | 0925 | 0926 | 0928 | 0931 | 0934 | 0936 | 0937 | 0938 |
|------------------------------|------|------|------|------|------|------|------|------|------|------|
| SKELETAL MUSCLE | N | N | N | N | N | N | N | N | N | N |
| SCIATIC NERVE | N | N | N | N | N | N | N | N | N | N |
| TESTES | N | N | | N | N | N | N | N | | N |
| Germinal epith, degeneration | - | - | - | - | - | - | - | - | 3 | - |
| Seminif tubules, giant cells | - | - | 1 | - | - | - | - | - | - | - |
| EPIDIDYMIS | N | N | N | N | N | N | N | N | | N |
| Hypospermia | - | - | - | - | - | - | - | - | 3 | - |
| TONGUE | N | N | N | N | N | N | N | N | N | N |
| DIAPHRAGM | | U | N | | N | N | N | | | N |
| Inflammation, acute | - | - | - | 1 | - | - | - | 2 | - | - |
| Inflammation, subacute | 3 | - | - | - | - | - | - | - | 3 | - |
| RIB | N | N | N | N | N | N | N | N | N | N |
| COSTOCHONDRAL JUNCTION | N | N | U | N | N | N | N | N | N | N |
| STERNUM | N | N | N | N | N | N | N | N | N | N |
| BONE MARROW | N | N | | N | | N | N | N | N | N |
| Pigment, hemosiderin | - | - | 1 | - | 1 | - | - | - | - | - |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 44

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4

SEX: MALE

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0921 | 0924 | 0925 | 0926 | 0928 | 0931 | 0934 | 0936 | 0937 | 0933 |
|-----------------|------|------|------|------|------|------|------|------|------|------|
| EYE | N | N | N | A | N | N | N | A | N | N |
| HARDERIAN GLAND | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 45

| ANIMAL ID: | 0801 | 0802 | 0806 | 0807 | 0809 | 0810 | 0811 | 0814 | 0815 | 0816 |
|--------------------------------|------|------|------|------|------|------|------|------|------|------|
| PITUITARY GLAND | | | | | | | | | | |
| Pars distalis, vacuo, cytopl | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 2 | 1 | 2 |
| Pars intermedia, cyst | - | - | - | - | - | - | P | - | - | - |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| LIVER | | N | N | N | N | N | | N | N | N |
| Lobular hyperplasia | 2 | - | - | - | - | - | - | - | - | - |
| Periportal, infiltr, cellular | - | - | - | - | - | - | 1 | - | - | - |
| SPLEEN | N | N | N | N | N | N | N | N | N | N |
| LUNG | N | N | N | | N | N | N | | N | |
| Hemorrhage | - | - | - | 1 | - | - | - | - | - | 1 |
| Inflammation, subacute | - | - | - | - | - | - | - | 1 | - | 1 |
| KIDNEY | N | N | | N | N | | N | N | | |
| Cortex, cyst | - | - | - | - | - | - | - | - | - | P |
| Nephropathy | - | - | 1 | - | - | - | - | - | 1 | - |
| Renal tubule, epith, regenerat | - | - | - | - | - | 1 | - | - | - | - |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 46

PROJECT ID: TRL098

GROUP: 2 - R

SEX: MALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0844 | 0846 | 0848 | 0850 | 0851 | 0852 | 0853 | 0858 | 0859 | 0860 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| LUNG | | N | | N | N | | | | | |
| Hemorrhage | - | - | - | - | - | 1 | 1 | - | 1 | 1 |
| Inflammation, subacute | 1 | - | 1 | - | - | - | - | 1 | - | - |
| Pigment, hemosiderin | - | - | - | - | - | - | - | - | - | 1 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 47

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3 - R
SEX: MALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0884 | 0887 | 0889 | 0890 | 0893 | 0895 | 0896 | 0897 | 0899 | 0900 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| LUNG | | | | | N | | | | | |
| Hemorrhage | - | - | 1 | - | - | - | - | - | - | 1 |
| Inflammation, chronic | - | 1 | - | 1 | - | 1 | 1 | - | 1 | - |
| Inflammation, subacute | - | - | 1 | 1 | - | - | - | 1 | - | - |
| Pigment, hemosiderin | 1 | 1 | - | 2 | - | 1 | 1 | 1 | 1 | - |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 48

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0922 | 0923 | 0927 | 0929 | 0930 | 0932 | 0933 | 0935 | 0939 | 0940 |
|---------------------------------|------|------|------|------|------|------|------|------|------|------|
| PITUITARY GLAND | | | | | | N | | | | |
| Pars distalis, hyperplasia | - | - | - | - | - | - | 1 | - | - | - |
| Pars distalis, vacuo, cytopl | 1 | 1 | 1 | 1 | 1 | - | 1 | 2 | 1 | 1 |
| Rathke's cleft, tubular hyperpl | - | - | - | - | - | - | - | 1 | - | - |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| LIVER | N | | N | N | N | N | N | N | N | N |
| Hepatocyte, vacuo, cytoplasm | - | 1 | - | - | - | - | - | - | - | - |
| SPLEEN | N | N | N | N | N | N | N | N | N | |
| Pigment, hemosiderin | - | - | - | - | - | - | - | - | - | 1 |
| LUNG | | | | | N | | | | | N |
| Alveolar epithelium, hyperpl | - | - | - | - | - | 1 | - | - | - | - |
| Alveolar hystiocytosis | - | - | 1 | - | - | 1 | 1 | - | - | - |
| Inflammation, chronic | - | - | - | - | - | - | 2 | - | - | - |
| Inflammation, subacute | 1 | 1 | - | - | - | - | - | - | - | - |
| Pigment, hemosiderin | 1 | 1 | 1 | 1 | - | 1 | 1 | 1 | 1 | - |
| KIDNEY | | N | N | N | | | N | N | N | |
| Infiltrate, cellular | - | - | - | - | 1 | - | - | - | - | - |
| Nephropathy | - | - | - | - | - | - | - | - | - | 1 |
| Pigment, hemosiderin | 1 | - | - | - | - | 1 | - | - | - | - |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 49

| ANIMAL ID: | 0821 | 0822 | 0825 | 0826 | 0828 | 0829 | 0832 | 0833 | 0838 | 0839 |
|-----------------------------|------|------|------|------|------|------|------|------|------|------|
| BRAIN | N | N | N | N | N | N | N | N | N | N |
| PITUITARY GLAND | N | N | N | N | N | | N | N | N | N |
| Pars distalis, cyst | - | - | - | - | - | P | - | - | - | - |
| SPINAL CORD, THORACIC | N | N | N | N | N | N | N | N | N | N |
| THYMUS | N | N | N | N | N | N | N | N | N | N |
| SALIVARY GLAND | N | N | N | N | N | N | N | N | N | N |
| PANCREAS | N | N | N | N | N | N | N | N | N | N |
| ADRENAL GLAND | N | N | N | N | N | N | N | | N | N |
| Cortex, cystic degeneration | - | - | - | - | - | - | - | 1 | - | - |
| TRACHEA | N | N | N | N | N | N | N | N | N | N |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| PARATHYROID GLAND | N | N | N | N | N | N | N | N | | U |
| Fibrosis | - | - | - | - | - | - | - | - | 2 | - |
| ESOPHAGUS | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 50

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0821 | 0822 | 0825 | 0826 | 0828 | 0829 | 0832 | 0833 | 0838 | 0839 |
|-----------------------------|------|------|------|------|------|------|------|------|------|------|
| HEART | N | N | N | N | | N | N | N | N | N |
| Hemorrhage | - | - | - | - | 1 | - | - | - | - | - |
| DUODENUM | N | N | N | N | N | N | N | N | N | N |
| COLON | N | N | N | N | N | N | N | N | N | N |
| STOMACH | N | N | N | | N | N | N | N | N | N |
| Non-glandular, inflammation | - | - | - | 1 | - | - | - | - | - | - |
| LIVER | N | N | N | N | N | | N | | | N |
| Inflammation, subacute | - | - | - | - | - | 1 | - | 1 | 1 | - |
| SPLEEN | N | N | N | N | N | N | N | N | N | N |
| JEJUNUM | N | N | N | N | N | N | N | N | N | N |
| LUNG | | | N | | N | N | N | N | N | N |
| Hemorrhage | - | 1 | - | - | - | - | - | - | - | - |
| Inflammation, subacute | 1 | - | - | 1 | - | - | - | - | - | - |
| KIDNEY | N | | | N | N | | | | | |
| Nephrocalcinosis | - | 1 | 1 | - | - | 2 | 1 | 1 | 1 | 2 |
| URINARY BLADDER | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 51

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0821 | 0822 | 0825 | 0826 | 0828 | 0829 | 0832 | 0833 | 0838 | 0839 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| SKIN | N | N | N | N | N | N | N | N | N | N |
| MAMMARY GLAND | U | N | N | N | N | N | N | N | N | N |
| ILEUM | N | N | N | N | N | N | N | N | N | N |
| CECUM | N | N | N | N | N | N | N | N | N | N |
| LYMPH NODE, MESENTERIC | N | N | N | N | N | N | N | N | N | N |
| SKELETAL MUSCLE | N | N | N | N | N | N | N | N | N | N |
| SCIATIC NERVE | N | N | N | N | N | N | N | N | N | N |
| OVARY | N | N | N | N | N | N | N | N | N | N |
| UTERUS | | N | N | | | N | | | | N |
| Decidua | 2 | - | - | - | - | - | - | - | - | - |
| Dilatation | - | - | - | 2 | - | - | - | 2 | 1 | - |
| Hemorrhage | - | - | - | - | 1 | - | - | - | - | - |
| Inflammation, acute | - | - | - | - | - | - | 1 | - | - | - |
| TONGUE | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 52

PROJECT ID: TRL098

GROUP: 1

SEX: FEMALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0821 | 0822 | 0825 | 0826 | 0828 | 0829 | 0832 | 0833 | 0838 | 0839 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| DIAPHRAGM | N | N | N | N | N | N | N | N | N | N |
| RIB | N | N | N | N | N | N | N | N | N | N |
| COSTOCHONDRAL JUNCTION | N | N | N | N | N | N | N | N | N | N |
| STERNUM | N | N | N | N | N | N | N | N | N | N |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |
| EYE | N | N | N | N | N | N | N | N | N | N |
| HARDERIAN GLAND | N | N | N | N | | N | N | N | N | N |
| Inflammation, subacute | - | - | - | - | 1 | - | - | - | - | - |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 53

PROJECT ID: TRL098

GROUP: 1

SEX: FEMALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

ANIMAL ID:

0821 0822 0825 0826 0828 0829 0832 0833 0838 0839

OTHER TISSUES AND LESIONS:

SKIN, HEAD - Inflamm, chronic

- - - - - 2 - - -

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 54

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0862 | 0863 | 0865 | 0866 | 0869 | 0870 | 0872 | 0875 | 0876 | 0878 |
|-------------------------------|------|------|------|------|------|------|------|------|------|------|
| PITUITARY GLAND | N | N | N | N | N | N | N | N | N | N |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| LIVER | | N | N | N | N | N | N | N | N | N |
| Basophilic focus | 1 | - | - | - | - | - | - | - | - | - |
| Periportal, infiltr, cellular | 1 | - | - | - | - | - | - | - | - | - |
| SPLEEN | N | N | N | N | N | N | N | N | N | N |
| LUNG | N | N | N | N | N | N | N | N | N | N |
| KIDNEY | N | | | N | | N | N | | | |
| Nephrocalcinosis | - | 1 | 1 | - | 1 | - | - | 1 | 1 | 1 |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3

SEX: FEMALE

FATES: Terminal Sacrifice, Natural Death

DRAFT

PAGE 55

| ANIMAL ID: | 0903 | 0905 | 0906 | 0907 | 0910 | 0911 | 0913 | 0914 | 0917 | 0920 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| PITUITARY GLAND | N | N | N | N | N | N | N | N | N | N |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| LIVER | N | N | N | N | | | | N | N | N |
| Infiltrate, cellular | - | - | - | - | 1 | 1 | 1 | - | - | - |
| Pigment, hemosiderin | - | - | - | - | 1 | 1 | - | - | - | - |
| SPLEEN | N | N | N | N | N | N | N | N | N | N |
| LUNG | | | | | | | | | | |
| Alveolar proteinosis | 2 | 2 | 1 | 2 | 2 | 2 | 1 | 1 | 1 | 2 |
| Inflammation, subacute | - | - | - | 1 | 1 | 1 | - | - | 1 | 1 |
| KIDNEY | | | N | | | | | N | N | |
| Nephrocalcinosis | 1 | 1 | - | 1 | 1 | - | 1 | - | - | - |
| Nephrosis, hemoglobin | - | - | - | 1 | 1 | - | 1 | - | - | 1 |
| Pigment, hemosiderin | - | - | - | 1 | - | 1 | - | - | - | - |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 56

PROJECT ID: TRL098

GROUP: 4

SEX: FEMALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0943 | 0945 | 0946 | 0947 | 0948 | 0950 | 0951 | 0952 | 0955 | 0958 |
|-----------------------------|------|------|------|------|------|------|------|------|------|------|
| BRAIN | N | N | N | N | N | N | N | N | N | N |
| PITUITARY GLAND | N | N | N | N | N | N | N | | N | N |
| Pars distalis, cyst | - | - | - | - | - | - | - | P | - | - |
| SPINAL CORD, THORACIC | N | N | N | N | N | N | N | N | N | N |
| THYMUS | N | N | N | N | N | N | N | N | N | N |
| SALIVARY GLAND | N | N | N | N | N | N | N | N | N | N |
| PANCREAS | N | N | N | N | N | N | N | N | N | N |
| ADRENAL GLAND | N | N | N | N | N | N | N | N | | |
| Cortex, pigment, lipofuscin | - | - | - | - | - | - | - | - | 1 | 1 |
| TRACHEA | N | N | N | N | N | N | N | N | N | N |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| PARATHYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| ESOPHAGUS | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 57

PROJECT ID: TRL098

GROUP: 4

SEX: FEMALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0943 | 0945 | 0946 | 0947 | 0948 | 0950 | 0951 | 0952 | 0955 | 0958 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| HEART | N | N | N | N | N | | N | | N | N |
| Cardiomyopathy | - | - | - | - | - | 1 | - | 1 | - | - |
| DUODENUM | N | N | N | N | N | N | N | N | N | N |
| COLON | N | N | N | N | N | N | N | N | N | N |
| STOMACH | N | N | N | N | N | N | N | N | N | N |
| LIVER | N | N | N | N | N | N | N | N | N | N |
| SPLEEN | | | | N | | | | N | | |
| Hyperplasia | 2 | 2 | 2 | - | 2 | 2 | 2 | - | 2 | 1 |
| JEJUNUM | N | N | N | N | N | N | N | N | N | N |
| LUNG | | | | | | | | | | |
| Alveolar proteinosis | 3 | 2 | 3 | 3 | 1 | 3 | 2 | 2 | 2 | 1 |
| Inflammation, acute | - | - | - | 1 | - | - | - | - | 1 | - |
| Inflammation, subacute | - | - | - | - | - | 1 | - | - | - | - |
| KIDNEY | | | | | | | | | | |
| Nephrocalcinosis | - | - | - | - | 1 | 1 | 1 | - | 1 | - |
| Nephrosis, hemoglobin | 1 | 2 | 2 | 1 | 2 | 1 | 2 | 1 | 2 | 1 |
| Pigment, hemosiderin | 2 | 3 | 2 | 2 | 2 | 2 | 3 | 2 | 2 | 2 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 58

PROJECT ID: TRL098

GROUP: 4

SEX: FEMALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0943 | 0945 | 0946 | 0947 | 0948 | 0950 | 0951 | 0952 | 0955 | 0958 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| URINARY BLADDER | N | N | N | N | N | N | N | N | N | N |
| SKIN | N | N | N | N | N | N | N | N | N | N |
| MAMMARY GLAND | N | N | N | N | N | N | N | N | N | N |
| ILEUM | N | N | N | N | N | N | N | N | N | N |
| CECUM | N | N | N | N | N | N | N | N | N | N |
| LYMPH NODE, MESENTERIC | N | N | N | N | N | N | N | N | N | N |
| SKELETAL MUSCLE | N | N | N | N | N | N | N | N | N | N |
| SCIATIC NERVE | N | N | N | N | N | N | N | N | N | N |
| OVARY | N | N | N | N | N | N | N | N | N | N |
| UTERUS | | | N | N | N | N | N | | N | N |
| Dilatation | 2 | 2 | - | - | - | - | - | 2 | - | - |
| TONGUE | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 59

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

| ANIMAL ID: | 0943 | 0945 | 0946 | 0947 | 0948 | 0950 | 0951 | 0952 | 0955 | 0958 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| DIAPHRAGM | N | N | N | N | N | N | N | N | N | N |
| RIB | N | N | N | N | N | N | N | N | N | N |
| COSTOCHONDRAL JUNCTION | N | N | N | N | N | N | N | N | N | N |
| STERNUM | N | N | N | N | N | N | N | N | N | N |
| BONE MARROW | N | | | N | N | | | | N | N |
| Pigment, hemosiderin | - | 1 | 1 | - | - | 1 | 1 | 1 | - | - |
| EYE | N | N | N | N | N | N | N | N | N | N |
| HARDERIAN GLAND | | N | N | N | N | N | N | N | N | N |
| Infiltrate, cellular | 1 | - | - | - | - | - | - | - | - | - |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 60

PROJECT ID: TRL098

GROUP: 4

SEX: FEMALE

WEEKS: 2-27

FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0943 | 0945 | 0946 | 0947 | 0948 | 0950 | 0951 | 0952 | 0955 | 0958 |
|---------------------------------|------|------|------|------|------|------|------|------|------|------|
| OTHER TISSUES AND LESIONS: | | | | | | | | | | |
| SKIN, EAR - Inflamm, granulomat | - | - | - | - | 4 | - | - | - | - | - |
| SKIN - Granuloma, foreign body | - | - | - | - | - | - | 3 | - | - | - |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 61

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0823 | 0824 | 0827 | 0830 | 0831 | 0834 | 0835 | 0836 | 0837 | 0840 |
|--------------------------------|------|------|------|------|------|------|------|------|------|------|
| PITUITARY GLAND | | N | N | N | N | N | U | | | |
| Pars distalis, adenoma | P | - | - | - | - | - | - | - | P | - |
| Pars distalis, vacuo, cytopl | - | - | - | - | - | - | - | 1 | - | 1 |
| Pars intermedia, cyst | P | - | - | - | - | - | - | - | - | - |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| LIVER | N | N | N | N | N | N | N | N | | N |
| Hepatocyte, vacuo, cytoplasm | - | - | - | - | - | - | - | - | 1 | - |
| SPLEEN | N | N | N | N | N | N | N | N | N | N |
| LUNG | N | N | N | N | N | N | N | N | N | N |
| KIDNEY | N | | | | N | | | N | | |
| Nephrocalcinosis | - | 1 | 1 | 1 | - | 1 | - | - | 1 | 1 |
| Renal tubule, casts, proteinic | - | - | - | - | - | - | 1 | - | - | - |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 62

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0861 | 0864 | 0867 | 0868 | 0871 | 0873 | 0874 | 0877 | 0879 | 0880 |
|------------|------|------|------|------|------|------|------|------|------|------|
| LUNG | N | N | N | N | N | N | | N | N | N |
| Hemorrhage | - | - | - | - | - | - | 1 | - | - | - |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 63

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0901 | 0902 | 0904 | 0908 | 0909 | 0912 | 0915 | 0916 | 0918 | 0919 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| LUNG | | | N | | | | | | | |
| Inflammation, chronic | 1 | 2 | - | 1 | - | - | 2 | 2 | 2 | 1 |
| Inflammation, subacute | - | - | - | 1 | - | - | - | - | - | - |
| Pigment, hemosiderin | 1 | 2 | - | - | 1 | 2 | 2 | 1 | 1 | 2 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 64

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0941 | 0942 | 0944 | 0949 | 0953 | 0954 | 0956 | 0957 | 0959 | 0960 |
|-----------------------|------|------|------|------|------|------|------|------|------|------|
| BRAIN | * | * | * | * | * | * | N | * | * | * |
| PITUITARY GLAND | N | N | N | N | N | N | N | N | N | N |
| SPINAL CORD, THORACIC | * | * | * | * | * | * | N | * | * | * |
| THYMUS | * | * | * | * | * | * | | * | * | * |
| Congestion | - | - | - | - | - | - | 1 | - | - | - |
| SALIVARY GLAND | * | * | * | * | * | * | N | * | * | * |
| PANCREAS | * | * | * | * | * | * | N | * | * | * |
| ADRENAL GLAND | * | * | * | * | * | * | N | * | * | * |
| TRACHEA | * | * | * | * | * | * | N | * | * | * |
| THYROID GLAND | N | N | N | N | N | N | N | N | N | N |
| PARATHYROID GLAND | * | * | * | * | * | * | U | * | * | * |
| ESOPHAGUS | * | * | * | * | * | * | N | * | * | * |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 65

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0941 | 0942 | 0944 | 0949 | 0953 | 0954 | 0956 | 0957 | 0959 | 0960 |
|-------------------------------|------|------|------|------|------|------|------|------|------|------|
| HEART | * | * | * | * | * | * | N | * | * | * |
| DUODENUM | * | * | * | * | * | * | N | * | * | * |
| COLON | * | * | * | * | * | * | N | * | * | * |
| STOMACH | * | * | * | * | * | * | N | * | * | * |
| LIVER | | N | | | N | N | N | N | | N |
| Bile duct, hyperplasia | 2 | - | 1 | 2 | - | - | - | - | 1 | - |
| Periportal, infiltr, cellular | - | - | 1 | - | - | - | - | - | - | - |
| Portal, fibrosis | 1 | - | - | - | - | - | - | - | - | - |
| SPLEEN | N | N | N | N | N | N | | N | | N |
| Pigment, hemosiderin | - | - | - | - | - | - | - | - | 1 | - |
| Serosa, inflammation, chronic | - | - | - | - | - | - | 2 | - | - | - |
| JEJUNUM | * | * | * | * | * | * | N | * | * | * |
| LUNG | | | | | | | | | | |
| Alveolar hystiocytosis | 1 | - | - | - | - | 1 | - | 1 | - | - |
| Alveolar proteinosis | - | - | - | - | - | - | 3 | - | - | - |
| Inflammation, chronic | 1 | - | - | - | 1 | 1 | - | 2 | - | 1 |
| Inflammation, subacute | - | - | - | - | - | - | 1 | - | - | - |
| Pigment, hemosiderin | 2 | 1 | 1 | 1 | 1 | 1 | - | 1 | 1 | 1 |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 66

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0941 | 0942 | 0944 | 0949 | 0953 | 0954 | 0956 | 0957 | 0959 | 0960 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| KIDNEY | | | N | N | | | | | | |
| Cortex, cyst | - | - | - | - | - | - | - | P | - | - |
| Nephrocalcinosis | 1 | 1 | - | - | 1 | 1 | 1 | 2 | 1 | 1 |
| Nephropathy | - | - | - | - | - | - | - | - | 1 | - |
| Pigment, hemosiderin | - | - | - | - | - | 1 | 2 | - | - | - |
| URINARY BLADDER | * | * | * | * | * | * | N | * | * | * |
| SKIN | * | * | * | * | * | * | N | * | * | * |
| MAMMARY GLAND | * | * | * | * | * | * | U | * | * | * |
| ILEUM | * | * | * | * | * | * | N | * | * | * |
| CECUM | * | * | * | * | * | * | N | * | * | * |
| LYMPH NODE, MESENTERIC | * | * | * | * | * | * | N | * | * | * |
| SKELETAL MUSCLE | * | * | * | * | * | * | N | * | * | * |
| SCIATIC NERVE | * | * | * | * | * | * | U | * | * | * |
| OVARY | * | * | * | * | * | * | N | * | * | * |

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Tabulated Animal Data

DRAFT

PAGE 67

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

| ANIMAL ID: | 0941 | 0942 | 0944 | 0949 | 0953 | 0954 | 0956 | 0957 | 0959 | 0960 |
|------------------------|------|------|------|------|------|------|------|------|------|------|
| UTERUS | * | * | * | * | * | * | N | * | * | * |
| TONGUE | * | * | * | * | * | * | N | * | * | * |
| DIAPHRAGM | * | * | * | * | * | * | N | * | * | * |
| RIB | * | * | * | * | * | * | N | * | * | * |
| COSTOCHONDRAL JUNCTION | * | * | * | * | * | * | N | * | * | * |
| STERNUM | * | * | * | * | * | * | N | * | * | * |
| BONE MARROW | N | N | N | N | N | N | N | N | N | N |
| EYE | * | * | * | * | * | * | N | * | * | * |
| HARDERIAN GLAND | * | * | * | * | * | * | N | * | * | * |

09-Sep-1993

SECTION V

CORRELATION OF GROSS AND MICROSCOPIC (MICRO) FINDINGS

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 69

ANIMAL ID: 0803 PATHOLOGY ID. NO: TI098-0803 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0804 PATHOLOGY ID. NO: TI098-0804 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0805 PATHOLOGY ID. NO: TI098-0805 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0808 PATHOLOGY ID. NO: TI098-0808 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 70

ANIMAL ID: 0812 PATHOLOGY ID. NO: TI098-0812 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0813 PATHOLOGY ID. NO: TI098-0813 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0817 PATHOLOGY ID. NO: TI098-0817 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0818 PATHOLOGY ID. NO: TI098-0818 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 71

ANIMAL ID: 0819 PATHOLOGY ID. NO: TI098-0819 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0820 PATHOLOGY ID. NO: TI098-0820 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 72

ANIMAL ID: 0841 PATHOLOGY ID. NO: TI098-0841 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0842 PATHOLOGY ID. NO: TI098-0842 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0843 PATHOLOGY ID. NO: TI098-0843 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SPLEEN - SMALL, 28X8 MM

No corresponding lesion

ANIMAL ID: 0845 PATHOLOGY ID. NO: TI098-0845 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 73

ANIMAL ID: 0847 PATHOLOGY ID. NO: TI098-0847 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0849 PATHOLOGY ID. NO: TI098-0849 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0854 PATHOLOGY ID. NO: TI098-0854 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0855 PATHOLOGY ID. NO: TI098-0855 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2
SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 74

ANIMAL ID: 0856 PATHOLOGY ID. NO: TI098-0856 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LIVER, PARENCHYMA - LESION, MOTTLED

No corresponding lesion

>ADRENAL GLAND, BILATERAL - SMALL,
1.5X2.0 MM

Not required by protocol

ANIMAL ID: 0857

PATHOLOGY ID. NO: TI098-0857 PATHOLOGIST: MJT

ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 75

ANIMAL ID: 0881 PATHOLOGY ID. NO: TI098-0881 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0882 PATHOLOGY ID. NO: TI098-0882 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE, FIRM

LUNG- Alveolar proteinosis

ANIMAL ID: 0883 PATHOLOGY ID. NO: TI098-0883 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 76

ANIMAL ID: 0885 PATHOLOGY ID. NO: TI098-0885 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0886 PATHOLOGY ID. NO: TI098-0886 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0888 PATHOLOGY ID. NO: TI098-0888 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

10-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 77

ANIMAL ID: 0891 PATHOLOGY ID. NO: TI098-0891 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SKIN, THORACIC, LEFT, SUBCUTANEOUS
TISSUE - MASS, SINGLE, PLAQUE,
16X12X9 MM

Not required by protocol

>TESTES, BILATERAL - SMALL

Not required by protocol

>EPIDIDYMIS, BILATERAL - SMALL

Not required by protocol

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0892 PATHOLOGY ID. NO: TI098-0892 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LYMPH NODE, MANDIBULAR - ENLARGED,
2, TAN, 8X5X5 MM

Not required by protocol

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 78

ANIMAL ID: 0894 PATHOLOGY ID. NO: TI098-0894 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

>ADRENAL GLAND, UNILATERAL - SMALL,
1.5X2.0 MM

Not required by protocol

ANIMAL ID: 0898 PATHOLOGY ID. NO: TI098-0898 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4
FATES: Terminal Secrifice, Natural Death

SEX: MALE

PAGE 79

ANIMAL ID: 0921
ANIMAL FATE: Natural Death

PATHOLOGY ID. NO: TI098-0921 PATHOLOGIST: MJT

WEEKS ON TEST:2

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>HEART, EPICARDIUM - LESION,
DIFFUSE, WHITE

HEART- Epicardium, inflam,
subacute

>LUNG, LEFT - DIFFUSE, BLACK

LUNG- Pleura, inflammation,
subacute

ANIMAL ID: 0924
ANIMAL FATE: Terminal Secrifice

PATHOLOGY ID. NO: TI098-0924 PATHOLOGIST: MJT

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0925
ANIMAL FATE: Terminal Secrifice

PATHOLOGY ID. NO: TI098-0925 PATHOLOGIST: MJT

WEEKS ON TEST:14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SPLEEN - ENLARGED

SPLEEN- Hyperplasia

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 80

ANIMAL ID: 0926
ANIMAL FATE: Natural Death

PATHOLOGY ID. NO: TI098-0926 PATHOLOGIST: MJT

WEEKS ON TEST: 2

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0928
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0928 PATHOLOGIST: MJT

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0931
ANIMAL FATE: Terminal Sacrifice

PATHOLOGY ID. NO: TI098-0931 PATHOLOGIST: MJT

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4
SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 81

ANIMAL ID: 0934
ANIMAL FATE: Natural Death

PATHOLOGY ID. NO: TI098-0934

PATHOLOGIST: MJT
WEEKS ON TEST:8

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0936
ANIMAL FATE: Natural Death

PATHOLOGY ID. NO: TI098-0936

PATHOLOGIST: MJT
WEEKS ON TEST:2

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0937
ANIMAL FATE: Natural Death

PATHOLOGY ID. NO: TI098-0937

PATHOLOGIST: MJT
WEEKS ON TEST:2

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>HEART, EPICARDIUM - LESION,
DIFFUSE, WHITE

HEART- Epicardium, inflam,
subacute

>LUNG, PLEURA - LESION, DIFFUSE,
WHITE

LUNG- Pleura, inflammation,
subacute

>TESTES, CAPSULE - FOCUS, RED

No corresponding lesion

10-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 32

ANIMAL ID: 0938

PATHOLOGY ID. NO: TI098-0938 PATHOLOGIST: MJT

ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1 - R
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 83

ANIMAL ID: 0801 PATHOLOGY ID. NO: TI098-0801 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LIVER, MEDIAN LOBE - MASS, 25X18X15 LIVER- Lobular hyperplasia
MM

ANIMAL ID: 0802 PATHOLOGY ID. NO: TI098-0802 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0806 PATHOLOGY ID. NO: TI098-0806 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0807 PATHOLOGY ID. NO: TI098-0807 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098 GROUP: 1 - R SEX: MALE PAGE 84
WEEKS: 2-27 FATES: Terminal Sacrifice, Natural Death

ANIMAL ID: 0809 PATHOLOGY ID. NO: TI098-0809 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 0810 PATHOLOGY ID. NO: TI098-0810 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 0811 PATHOLOGY ID. NO: TI098-0811 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>KIDNEY, BILATERAL - LESION, No corresponding lesion
MULTIPLE, IRREGULAR, MOTTLED

ANIMAL ID: 0814 PATHOLOGY ID. NO: TI098-0814 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>LUNG, DIAPHRAGMATIC LOBE - LESION, No corresponding lesion
DIFFUSE, PALE

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1 - R
FATES: Terminal Sacrifice, Natural Death

SEX: MALE

PAGE 85

ANIMAL ID: 0815 PATHOLOGY ID. NO: TI098-0815 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0816 PATHOLOGY ID. NO: TI098-0816 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 86

ANIMAL ID: 0844 PATHOLOGY ID. NO: TI098-0844 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0846 PATHOLOGY ID. NO: TI098-0846 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0848 PATHOLOGY ID. NO: TI098-0848 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0850 PATHOLOGY ID. NO: TI098-0850 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 87

ANIMAL ID: 0851 PATHOLOGY ID. NO: TI098-0851 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0852 PATHOLOGY ID. NO: TI098-0852 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0853 PATHOLOGY ID. NO: TI098-0853 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0858 PATHOLOGY ID. NO: TI098-0858 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2 - R SEX: MALE PAGE 88
FATES: Terminal Sacrifice, Natural Death

ANIMAL ID: 0859 PATHOLOGY ID. NO: TI098-0859 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 0860 PATHOLOGY ID. NO: TI098-0860 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>KIDNEY, BILATERAL - LESION, MOTTLED Not required by protocol

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 89

ANIMAL ID: 0884 PATHOLOGY ID. NO: TI098-0884 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0887 PATHOLOGY ID. NO: TI098-0887 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0889 PATHOLOGY ID. NO: TI098-0889 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0890 PATHOLOGY ID. NO: TI098-0890 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 90

ANIMAL ID: 0893 PATHOLOGY ID. NO: TI098-0893 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0895 PATHOLOGY ID. NO: TI098-0895 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0896 PATHOLOGY ID. NO: TI098-0896 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0897 PATHOLOGY ID. NO: TI098-0897 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>KIDNEY, BILATERAL - LESION,
MULTIPLE, IRREGULAR, MOTTLED

Not required by protocol

09-Sep-1993

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 91

ANIMAL ID: 0899 PATHOLOGY ID. NO: TI098-0899 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>EYE, RIGHT - LESION, OPAQUE

Not required by protocol

ANIMAL ID: 0900 PATHOLOGY ID. NO: TI098-0900 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 92

ANIMAL ID: 0922 PATHOLOGY ID. NO: TI098-0922 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0923 PATHOLOGY ID. NO: TI098-0923 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0927 PATHOLOGY ID. NO: TI098-0927 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0929 PATHOLOGY ID. NO: TI098-0929 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 93

ANIMAL ID: 0930 PATHOLOGY ID. NO: TI098-0930 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0932 PATHOLOGY ID. NO: TI098-0932 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0933 PATHOLOGY ID. NO: TI098-0933 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0935 PATHOLOGY ID. NO: TI098-0935 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: MALE
FATES: Terminal Sacrifice, Natural Death

PAGE 94

ANIMAL ID: 0939 PATHOLOGY ID. NO: TI098-0939 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0940 PATHOLOGY ID. NO: TI098-0940 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>MESENTERY, FAT - LESION, SINGLE,
OVAL, RED, 8X6X2 MM

Not required by protocol

09-Sep-1993

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

PAGE 95

ANIMAL ID: 0821 PATHOLOGY ID. NO: TI098-0821 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>UTERUS, BILATERAL - DIVERTICULUM, UTERUS- Deciduoma
MULTIPLE, OVAL

ANIMAL ID: 0822 PATHOLOGY ID. NO: TI098-0822 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 0825 PATHOLOGY ID. NO: TI098-0825 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 0826 PATHOLOGY ID. NO: TI098-0826 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 96

ANIMAL ID: 0828 PATHOLOGY ID. NO: TI098-0828 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0829 PATHOLOGY ID. NO: TI098-0829 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0832 PATHOLOGY ID. NO: TI098-0832 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SKIN, HEAD - SCAR, 20X15 MM

SKIN, HEAD - Inflammation, chronic

ANIMAL ID: 0833 PATHOLOGY ID. NO: TI098-0833 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>UTERUS, BILATERAL - DILATATION

UTERUS - Dilatation

10-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 97

ANIMAL ID: 0838 PATHOLOGY ID. NO: TI098-0838 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0839 PATHOLOGY ID. NO: TI098-0839 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 98

ANIMAL ID: 0862 PATHOLOGY ID. NO: TI098-0862 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0863 PATHOLOGY ID. NO: TI098-0863 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0865 PATHOLOGY ID. NO: TI098-0865 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0866 PATHOLOGY ID. NO: TI098-0866 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 99

ANIMAL ID: 0869 PATHOLOGY ID. NO: TI098-0869 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0870 PATHOLOGY ID. NO: TI098-0870 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0872 PATHOLOGY ID. NO: TI098-0872 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0875 PATHOLOGY ID. NO: TI098-0875 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>UTERUS, BILATERAL - DILATATION

Not required by protocol

09-Sep-1993

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098 GROUP: 2 SEX: FEMALE PAGE 100
WEEKS: 2-27 FATES: Terminal Sacrifice, Natural Death

ANIMAL ID: 0876 PATHOLOGY ID. NO: TI098-0876 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 0878 PATHOLOGY ID. NO: TI098-0878 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

09-Sep-1993

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 101

ANIMAL ID: 0903 PATHOLOGY ID. NO: TI098-0903 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0905 PATHOLOGY ID. NO: TI098-0905 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0906 PATHOLOGY ID. NO: TI098-0906 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 102

ANIMAL ID: 0907 PATHOLOGY ID. NO: TI098-0907 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0910 PATHOLOGY ID. NO: TI098-0910 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0911 PATHOLOGY ID. NO: TI098-0911 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE, FIRM

LUNG- Alveolar proteinosis

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 103

ANIMAL ID: 0913 PATHOLOGY ID. NO: TI098-0913 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

ANIMAL ID: 0914 PATHOLOGY ID. NO: TI098-0914 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0917 PATHOLOGY ID. NO: TI098-0917 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 107

ANIMAL ID: 0951 PATHOLOGY ID. NO: TI098-0951 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SKIN, SUBCUTANEOUS TISSUE - MASS,
SINGLE, PLAQUE, TAN, 3X4 MM

SKIN - Granuloma, foreign body

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE, FIRM

LUNG- Alveolar proteinosis

ANIMAL ID: 0952 PATHOLOGY ID. NO: TI098-0952 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE, FIRM

LUNG- Alveolar proteinosis

ANIMAL ID: 0955 PATHOLOGY ID. NO: TI098-0955 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4
FATES: Terminal Secrifice, Natural Death

SEX: FEMALE

PAGE 108

ANIMAL ID: 0958

PATHOLOGY ID. NO: TI098-0958 PATHOLOGIST: MJT

ANIMAL FATE: Terminal Secrifice

WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Alveolar proteinosis

10-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

PAGE 109

ANIMAL ID: 0823 PATHOLOGY ID. NO: TI098-0823 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0824 PATHOLOGY ID. NO: TI098-0824 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0827 PATHOLOGY ID. NO: TI098-0827 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0830 PATHOLOGY ID. NO: TI098-0830 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1 - R
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 110

ANIMAL ID: 0831 PATHOLOGY ID. NO: TI098-0831 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0834 PATHOLOGY ID. NO: TI098-0834 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0835 PATHOLOGY ID. NO: TI098-0835 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0836 PATHOLOGY ID. NO: TI098-0836 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 1 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

PAGE 111

ANIMAL ID: 0837 PATHOLOGY ID. NO: TI098-0837 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>PITUITARY GLAND - ENLARGED, 5X4 MM

PITUITARY GLAND- Pars distalis,
adenoma

ANIMAL ID: 0840 PATHOLOGY ID. NO: TI098-0840 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 2 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

PAGE 112

ANIMAL ID: 0861 PATHOLOGY ID. NO: TI098-0861 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0864 PATHOLOGY ID. NO: TI098-0864 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0867 PATHOLOGY ID. NO: TI098-0867 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0868 PATHOLOGY ID. NO: TI098-0868 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>EYE, RIGHT - LESION, OPAQUE

Not required by protocol

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098 GROUP: 2 - R SEX: FEMALE PAGE 113
WEEKS: 2-27 FATES: Terminal Sacrifice, Natural Death

ANIMAL ID: 0871 PATHOLOGY ID. NO: TI098-0871 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>EAR, BILATERAL - LESION Not required by protocol

ANIMAL ID: 0873 PATHOLOGY ID. NO: TI098-0873 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 0874 PATHOLOGY ID. NO: TI098-0874 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 0877 PATHOLOGY ID. NO: TI098-0877 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098 GROUP: 2 - R SEX: FEMALE PAGE 114
WEEKS: 2-27 FATES: Terminal Sacrifice, Natural Death

ANIMAL ID: 0879 PATHOLOGY ID. NO: TI098-0879 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 0880 PATHOLOGY ID. NO: TI098-0880 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>LIVER, CAPSULE - MASS, SINGLE, Not required by protocol
OVAL, WHITE, 1X2 MM

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

PAGE 115

ANIMAL ID: 0901 PATHOLOGY ID. NO: TI098-0901 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0902 PATHOLOGY ID. NO: TI098-0902 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0904 PATHOLOGY ID. NO: TI098-0904 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

PAGE 116

ANIMAL ID: 0908 PATHOLOGY ID. NO: TI098-0908 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>UTERUS, BILATERAL - DILATATION

Not required by protocol

ANIMAL ID: 0909 PATHOLOGY ID. NO: TI098-0909 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0912 PATHOLOGY ID. NO: TI098-0912 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>PITUITARY GLAND - ENLARGED

Not required by protocol

09-Sep-1993

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WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3 - R SEX: FEMALE
FATES: Terminal Secrifice, Natural Death

PAGE 117

ANIMAL ID: 0915 PATHOLOGY ID. NO: TI098-0915 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Secrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0916 PATHOLOGY ID. NO: TI098-0916 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Secrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0918 PATHOLOGY ID. NO: TI098-0918 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Secrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>EYE, LEFT - LESION, 1, OPAQUE

Not required by protocol

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Inflammation, chronic

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 3 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

PAGE 118

ANIMAL ID: 0919 PATHOLOGY ID. NO: TI098-0919 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Inflammation, chronic

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

PAGE 119

ANIMAL ID: 0941 PATHOLOGY ID. NO: TI098-0941 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0942 PATHOLOGY ID. NO: TI098-0942 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0944 PATHOLOGY ID. NO: TI098-0944 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0949 PATHOLOGY ID. NO: TI098-0949 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

09-Sep-1993

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R SEX: FEMALE
FATES: Terminal Sacrifice, Natural Death

PAGE 120

ANIMAL ID: 0953 PATHOLOGY ID. NO: TI098-0953 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0954 PATHOLOGY ID. NO: TI098-0954 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0956 PATHOLOGY ID. NO: TI098-0956 PATHOLOGIST: MJT
ANIMAL FATE: Natural Death

WEEKS ON TEST: 16

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, WHITE

LUNG- Alveolar proteinosis

09-Sep-1993

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 098

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL098
WEEKS: 2-27

GROUP: 4 - R
FATES: Terminal Sacrifice, Natural Death

SEX: FEMALE

PAGE 121

ANIMAL ID: 0957 PATHOLOGY ID. NO: TI098-0957 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>LUNG, PLEURA - LESION, MULTIPLE,
IRREGULAR, WHITE

LUNG- Inflammation, chronic

ANIMAL ID: 0959 PATHOLOGY ID. NO: TI098-0959 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

ANIMAL ID: 0960 PATHOLOGY ID. NO: TI098-0960 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice

WEEKS ON TEST: 27

REFERENCE TO NECROPSY RECORD:

RELATED HISTOPATHOLOGY:

>SPLEEN, CAPSULE - CYST, SINGLE,
LOBULATED, CLEAR, WATERY

No corresponding lesion

09-Sep-1993

SECTION VI
QUALITY ASSURANCE STATEMENT

QUALITY ASSURANCE STATEMENT

DRAFT

This histopathology project was inspected and audited by the PAI Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) regulations promulgated by the U.S. Food and Drug Administration. Results of these activities indicate that the portions of the study performed by PAI conformed with GLP regulations and applicable Standard Operating Procedures. The pathology narrative report is an accurate reflection of the recorded data. The following table is a record of the inspections/audits performed and reported by the QAU:

| Date of Inspection | Phase Inspected | Date Findings Reported to Management and Study Pathologist |
|--------------------|-------------------------------|--|
| * 04/22/93 | Tissue Trimming | 04/22/93 |
| * 06/08/93 | Processing/Embedding | 06/08/93 |
| ** 04/15/93 | Microtomy | 04/15/93 |
| * 07/14/93 | Staining | 07/19/93 |
| * 07/14/93 | Coverslipping | 07/19/93 |
| * 04/15/93 | Labeling | 04/15/93 |
| * 06/09/93 | Quality Control/Checkout | 06/09/93 |
| ** 09/10/93 | Individual Animal Data | 09/10/93 |
| ** 09/10/93 | Data Entry | 09/10/93 |
| ** 09/10/93 | Computer-Generated Tables | 09/10/93 |
| ** 09/10/93 | Draft Pathology Report | 09/10/93 |
| ** 09/28/93 | Second Draft Pathology Report | 09/28/93 |

*General quarterly phase inspection

**Inspection specific for Study Number

In accordance with the PAI Quality Assurance Division's Standard Operating Procedures, all critical phase inspections are conducted on a random basis quarterly or more frequently. Those general phase inspections listed are the most recent conducted during the period each task associated with this project was performed.



Quality Assurance Unit
PAI Illinois Division

09/28/93

Date

Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats, TRL Study Number 098.



Pathology Associates, Inc.

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BONE MARROW EVALUATION REPORT FOR

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

STUDY NUMBER 098

PREPARED FOR
TOXICOLOGY RESEARCH LABORATORY
CHICAGO, ILLINOIS

TABLE OF CONTENTS

DRAFT

| | |
|----------------------------------|-----|
| Bone Marrow Evaluation Narrative | I |
| M:E Ratio Group Summary Tables | II |
| Individual Animal M:E Ratio Data | III |
| Individual Animal Data Sheets | IV |
| Quality Assurance Statement | V |

DRAFT

I. Bone Marrow Evaluation Narrative

BONE MARROW EVALUATION REPORT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605 WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INTRODUCTION

This report prepared by Pathology Associates, Inc. (PAI) for Toxicology Research Laboratory (TRL), University of Illinois at Chicago, Department of Pharmacology, P. O. Box 6998, Chicago, IL, 60680, presents the results of bone marrow evaluation from rats given WR 238605 orally by gavage once daily for at least thirteen weeks.

EXPERIMENTAL DESIGN AND METHODS

Eighty male and eighty female rats were randomized into one of four groups as described below.

| Treatment Group | Dose Level (mg base/kg/day) | Number of Males | Number of Females |
|-----------------|-----------------------------|-----------------|-------------------|
| 1 | 0 | 10 + 10* | 10 + 10* |
| 2 | 0.5 | 10 + 10* | 10 + 10* |
| 3 | 6.0 | 10 + 10* | 10 + 10* |
| 4 | 18.0 | 10 + 10* | 10 + 10* |

*Recovery Animals.

Surviving animals designated for the Day 91 and 92 necropsies were necropsied in random order on Days 91 and 92. The remainder of the animals were held for a thirteen week recovery period at which time they were necropsied.

Bone marrow smears were prepared (and fixed in methanol) from the femur of each animal at all necropsies. The bone marrow smears from animals in the high dose (Group 4) and control (Group 1) groups were stained with a Modified Giemsa stain and evaluated microscopically to determine the Myeloid:Erythroid (M:E) Ratio. The M:E Ratio was determined on a cell count of 500 cells. Five high dose male animals (#0921, #0926, #0934, #0936 and #0937) died prior to the Day 91/92 necropsies and bone marrow smears were not prepared for these animals.

Statistical analysis of the data was performed by TRL and provided to PAI for inclusion in this report.

RESULTS

M:E Ratio Group Summary tables are presented in Section II (generated by TRL from PAI data sheets). Individual animal M:E Ratio data are presented by sex and dose group in Section III (generated by TRL from PAI data sheets). PAI-generated individual animal data sheets are presented by dose group and sex in Section IV.

The M:E Ratios from bone marrow smears collected from male and female high dose and control animals on Days 91 and 92 in this study were within normal limits.

CONCLUSION

Under the conditions of this study, WR 238605 did not result in a treatment-related effect in the M:E Ratio of the femoral bone marrow of male and female treated rats at Days 91 and 92.

Lynda L. Pippin, DVM
June 14, 1993

DRAFT

II. M:E Ratio Group Summary Tables

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

SUMMARY REPORT
TEST: M:E RATIO

STUDY: 098
STUDY NO: 098BM

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Week 14

Group: 1F : 0 mg base/kg/day
MEAN 1.59
SD 0.062
N 10

Group: 2F : 0.5 mg base/kg/day
MEAN NA
SD NA
N 0

Group: 3F : 6.0 mg base/kg/day
MEAN NA
SD NA
N 0

Group: 4F : 18.0 mg base/kg/day
MEAN 1.59
SD 0.074
N 10

DRAFT

NA-Not Applicable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

SUMMARY REPORT
TEST: M:E RATIO

STUDY: 098
STUDY NO: 098BM

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

PERIOD(s): Week 14

Group: 1M : 0 mg base/kg/day
MEAN 1.55
SD 0.066
N 10

Group: 2M : 0.5 mg base/kg/day
MEAN NA
SD NA
N 0

Group: 3M : 6.0 mg base/kg/day
MEAN NA
SD NA
N 0

Group: 4M : 18.0 mg base/kg/day
MEAN 1.55
SD 0.066
N 5

DRAFT

NA-Not Applicable

DRAFT

III. Individual Animal M:E Ratio Data

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 098
STUDY NO: 098BM
ABBR: M:E RATIO

SEX: MALE

UNITS: -

ANIMAL ID Week 14

GROUP: 1M:0 mg base/kg/day

| | |
|-----|------|
| 801 | -- |
| 802 | -- |
| 803 | 1.59 |
| 804 | 1.48 |
| 805 | 1.66 |
| 806 | -- |
| 807 | -- |
| 808 | 1.50 |
| 809 | -- |
| 810 | -- |
| 811 | -- |
| 812 | 1.55 |
| 813 | 1.46 |
| 814 | -- |
| 815 | -- |
| 816 | -- |
| 817 | 1.60 |
| 818 | 1.51 |
| 819 | 1.63 |
| 820 | 1.54 |

| | |
|------|-------|
| MEAN | 1.55 |
| SD | 0.066 |
| N | 10 |

DRAFT

GROUP: 2M:0.5 mg base/kg/day

| | |
|-----|----|
| 841 | -- |
| 842 | -- |
| 843 | -- |
| 844 | -- |
| 845 | -- |
| 846 | -- |
| 847 | -- |
| 848 | -- |
| 849 | -- |
| 850 | -- |
| 851 | -- |
| 852 | -- |
| 853 | -- |
| 854 | -- |
| 855 | -- |
| 856 | -- |
| 857 | -- |
| 858 | -- |
| 859 | -- |
| 860 | -- |

| | |
|------|----|
| MEAN | NA |
| SD | NA |
| N | 0 |

(--)-Data Unavailable

NA-Not Applicable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 098
STUDY NO: 0988M
ABBR: M:E RATIO

SEX: MALE

UNITS: -

ANIMAL ID Week 14

GROUP: 3M:6.0 mg base/kg/day

| | |
|-----|----|
| 881 | -- |
| 882 | -- |
| 883 | -- |
| 884 | -- |
| 885 | -- |
| 886 | -- |
| 887 | -- |
| 888 | -- |
| 889 | -- |
| 890 | -- |
| 891 | -- |
| 892 | -- |
| 893 | -- |
| 894 | -- |
| 895 | -- |
| 896 | -- |
| 897 | -- |
| 898 | -- |
| 899 | -- |
| 900 | -- |

| | |
|------|----|
| MEAN | NA |
| SD | NA |
| N | 0 |

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GROUP: 4M:18.0 mg base/kg/day

| | |
|-----|------|
| 921 | -- |
| 922 | -- |
| 923 | -- |
| 924 | 1.65 |
| 925 | 1.49 |
| 926 | -- |
| 927 | -- |
| 928 | 1.53 |
| 929 | -- |
| 930 | -- |
| 931 | 1.50 |
| 932 | -- |
| 933 | -- |
| 934 | -- |
| 935 | -- |
| 936 | -- |
| 937 | -- |
| 938 | 1.58 |
| 939 | -- |
| 940 | -- |

| | |
|------|-------|
| MEAN | 1.55 |
| SD | 0.066 |
| N | 5 |

(--)-Data Unavailable

NA-Not Applicable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 098
STUDY NO: 0988M
ASBR: M:E RATIO

SEX: FEMALE

UNITS: -

ANIMAL ID Week 14

GROUP: 1F:0 mg base/kg/day

| | |
|-----|------|
| 821 | 1.63 |
| 822 | 1.53 |
| 823 | -- |
| 824 | -- |
| 825 | 1.58 |
| 826 | 1.67 |
| 827 | -- |
| 828 | 1.55 |
| 829 | 1.49 |
| 830 | -- |
| 831 | -- |
| 832 | 1.65 |
| 833 | 1.54 |
| 834 | -- |
| 835 | -- |
| 836 | -- |
| 837 | -- |
| 838 | 1.56 |
| 839 | 1.66 |
| 840 | -- |

| | |
|------|-------|
| MEAN | 1.59 |
| SD | 0.062 |
| N | 10 |

DRAFT

GROUP: 2F:0.5 mg base/kg/day

| | |
|-----|----|
| 861 | -- |
| 862 | -- |
| 863 | -- |
| 864 | -- |
| 865 | -- |
| 866 | -- |
| 867 | -- |
| 868 | -- |
| 869 | -- |
| 870 | -- |
| 871 | -- |
| 872 | -- |
| 873 | -- |
| 874 | -- |
| 875 | -- |
| 876 | -- |
| 877 | -- |
| 878 | -- |
| 879 | -- |
| 880 | -- |

| | |
|------|----|
| MEAN | NA |
| SD | NA |
| N | 0 |

(--)-Data Unavailable

NA-Not Applicable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: M:E RATIO

STUDY ID: 098
STUDY NO: 0988M
ASBR: M:E RATIO

SEX: FEMALE

UNITS: -

ANIMAL ID Week 14

GROUP: 3F:6.0 mg base/kg/day

| | |
|-----|----|
| 901 | -- |
| 902 | -- |
| 903 | -- |
| 904 | -- |
| 905 | -- |
| 906 | -- |
| 907 | -- |
| 908 | -- |
| 909 | -- |
| 910 | -- |
| 911 | -- |
| 912 | -- |
| 913 | -- |
| 914 | -- |
| 915 | -- |
| 916 | -- |
| 917 | -- |
| 918 | -- |
| 919 | -- |
| 920 | -- |

| | |
|------|----|
| MEAN | NA |
| SD | NA |
| N | 0 |

DRAFT

GROUP: 4F:18.0 mg base/kg/day

| | |
|-----|------|
| 941 | -- |
| 942 | -- |
| 943 | 1.63 |
| 944 | -- |
| 945 | 1.51 |
| 946 | 1.66 |
| 947 | 1.56 |
| 948 | 1.46 |
| 949 | -- |
| 950 | 1.67 |
| 951 | 1.56 |
| 952 | 1.62 |
| 953 | -- |
| 954 | -- |
| 955 | 1.53 |
| 956 | -- |
| 957 | -- |
| 958 | 1.67 |
| 959 | -- |
| 960 | -- |

| | |
|------|-------|
| MEAN | 1.59 |
| SD | 0.074 |
| N | 10 |

(--)-Data Unavailable

NA-Not Applicable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

SUMMARY REPORT
TEST: M:E RATIO

STUDY: 098
STUDY NO: 098BM

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 14

| Group | N | Total | Mean | Std. Dev. | DUNNETT'S 't' | DUNNETT'S RANGES | | Source | Degree Fdm | Sum of Squares | Mean Square |
|--|----|-------|------|-----------|------------------|------------------|----|------------|---------------|-------------------|----------------|
| | | | | | | LO -95%- | HI | | | | |
| 1M | 10 | 15.52 | 1.55 | 0.066 | | | | TREATMENTS | 3 | 0.0000 | 0.0000 |
| 2M | NA | 0.00 | 0.00 | NA | | | | ERROR | 13 | 0.0572 | 0.0044 |
| 3M | NA | 0.00 | 0.00 | NA | | | | | | | |
| 4M | 5 | 7.75 | 1.55 | 0.066 | | | | TOTAL | 16 | 0.0572 | |
| F Ratio = 0.00 'F' table values F.01 = 9.07 F.05 = 4.67 | | | | | | | | | | | |
| Coeff. Var. % = 4.274 Dunnett's 'T' table values P.01 = 3.01 P.05 = 2.16 | | | | | | | | | | | |

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NA-Not Applicable

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

SUMMARY REPORT
TEST: M:E RATIO

STUDY: 098
STUDY NO: 098BM

SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

Week 14

| Group | N | Total | Mean | Std. Dev. | DUNNETT'S 't' | DUNNETT'S RANGES | | Source | Degree Fdn | Sum of Squares | Mean Square |
|--|----|-------|------|-----------|---------------|------------------|-------------|------------|------------|----------------|-------------|
| | | | | | | LO -95%- HI | LO -99%- HI | | | | |
| 1F | 10 | 15.86 | 1.59 | 0.062 | | | | TREATMENTS | 3 | 0.0000 | 0.0000 |
| 2F | NA | 0.00 | 0.00 | NA | | | | ERROR | 18 | 0.0839 | 0.0047 |
| 3F | NA | 0.00 | 0.00 | NA | | | | | | | |
| 4F | 10 | 15.87 | 1.59 | 0.074 | | | | TOTAL | 21 | 0.0839 | |
| F Ratio = 0.00 'F' table values F.01 = 8.28 F.05 = 4.41 | | | | | | | | | | | |
| Coeff. Var. % = 4.302 Dunnett's 'T' table values P.01 = 2.88 P.05 = 2.10 | | | | | | | | | | | |

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NA-Not Applicable

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IV. Individual Animal Data Sheets

INDIVIDUAL BONE MARROW M:E RATIO DATA

Group 1

Vehicle Control: 0 mg base/kg/day

| ANIMAL NO. | 0821 | 0822 | 0825 | 0826 | 0828 | 0829 | 0832 | 0833 | 0838 | 0839 |
|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| | 310:190 | 302:198 | 306:194 | 313:187 | 304:196 | 299:201 | 311:189 | 303:197 | 305:195 | 312:188 |
| RATIO | 1.63:1.00 | 1.53:1.00 | 1.58:1.00 | 1.67:1.00 | 1.55:1.00 | 1.49:1.00 | 1.65:1.00 | 1.54:1.00 | 1.56:1.00 | 1.66:1.00 |

Group 4

High-Dose: 18.0 mg base/kg/day

| ANIMAL NO. | 0943 | 0945 | 0946 | 0947 | 0948 | 0950 | 0951 | 0952 | 0955 | 0958 |
|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| | 310:190 | 301:199 | 312:188 | 305:195 | 297:203 | 313:187 | 305:195 | 309:191 | 302:198 | 313:187 |
| RATIO | 1.63:1.00 | 1.51:1.00 | 1.66:1.00 | 1.56:1.00 | 1.46:1.00 | 1.67:1.00 | 1.56:1.00 | 1.62:1.00 | 1.53:1.00 | 1.67:1.00 |

INDIVIDUAL BONE MARROW M:E RATIO DATA

Group 1

Vehicle Control: 0 mg base/kg/day

| ANIMAL NO. | 0803 | 0804 | 0805 | 0808 | 0812 | 0813 | 0817 | 0818 | 0819 | 0820 |
|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| | 307:193 | 298:202 | 312:188 | 300:200 | 304:196 | 297:203 | 308:192 | 301:199 | 310:190 | 303:197 |
| RATIO | 1.59:1.00 | 1.48:1.00 | 1.66:1.00 | 1.50:1.00 | 1.55:1.00 | 1.46:1.00 | 1.60:1.00 | 1.51:1.00 | 1.63:1.00 | 1.54:1.00 |

Group 4

High-Dose: 18.0 mg base/kg/day

| ANIMAL NO. | 0921 | 0924 | 0925 | 0926 | 0928 | 0931 | 0934 | 0936 | 0937 | 0938 |
|------------|------|-----------|-----------|------|-----------|-----------|------|------|------|-----------|
| | ED | 311:189 | 299:201 | ED | 302:198 | 300:200 | ED | ED | ED | 306:194 |
| RATIO | | 1.65:1.00 | 1.49:1.00 | | 1.53:1.00 | 1.50:1.00 | | | | 1.58:1.00 |

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V. Quality Assurance Statement



Pathology Associates, Inc.

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(301) 663-1644
(301) 663-8994 FAX

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QUALITY ASSURANCE STATEMENT

This histopathology project with the exception of statistical analysis tables (Sections II and III) provided by the testing facility, Toxicology Research Laboratory (TRL), has been inspected and audited by the PAI Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) regulations promulgated by the U.S. Food and Drug Administration. Results of these activities indicate that the portions of the study performed by PAI conformed with GLP regulations and applicable Standard Operating Procedures. The pathology narrative report is an accurate reflection of the recorded data. The following table is a record of the inspections/audits performed and reported by the QAU.

| <u>Date of Inspection</u> | <u>Phase Inspected</u> | <u>Date Findings Reported to Management/ Study Pathologist</u> |
|---------------------------|-------------------------------------|--|
| 06/14/93 | Individual Animal Data Sheets | 06/14/93 |
| 06/14/93 | Individual M:E Ratio Tables | 06/14/93 |
| 06/14/93 | Draft Bone Marrow Evaluation Report | 06/14/93 |

Carol C. Hoffman

Quality Assurance Specialist

06/29/93

Date

TRL Study No. 098
Thirteen Week Oral Toxicity Study of WR 238605 With a Thirteen Week Recovery Period in Rats

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Appendix 11
Pre-test Clinical Pathology Data

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

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PRETEST ANIMAL CLINICAL CHEMISTRY REPORT
PERIOD: PRETEST

| STUDY ID: 098P | | | | | | | SEX: MALE | |
|----------------|------------|------------|------------|-------------|--------------|-------------|------------|-----------|
| ANIMAL ID | ALT U/L | AST U/L | TP g/dL | ALB g/dL | TBA mg/dL | ALKP U/L | LDH U/L | CK U/L |
| GROUP: PRETEST | | | | | | | | |
| 18 | 67 | 104 | 6.1 | 3.5 | 89.0 | 276 | 291 | 183 |
| 45 | 72 | 122 | 7.0 | 3.9 | 99.2 | 388 | 88 | 261 |
| 48 | 87 | 122 | 6.8 | 3.7 | 41.1 | 291 | 96 | 241 |
| 56 | 74 | 115 | 6.8 | 3.9 | 146.9 | 266 | 270 | 284 |
| 75 | 95 | QNS | 7.4 | 4.0 | 237.7 | 304 | 98 | 202 |
| MEAN | 79 | 116 | 6.8 | 3.8 | 122.8 | 305 | 169 | 234 |
| SD | 11.6 | 8.5 | 0.47 | 0.20 | 74.43 | 48.6 | 102.5 | 41.5 |
| N | 5 | 4 | 5 | 5 | 5 | 5 | 5 | 5 |

nl = 25-200

QNS-Quantity Not Sufficient

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

PRETEST ANIMAL CLINICAL CHEMISTRY REPORT
PERIOD: PRETEST

STUDY ID: 098P

SEX: MALE

| ANIMAL ID | BUN mg/dL | CREA mg/dL | NA mmol/L | K mmol/L | CL mEq/L | CA mg/dL | IP mg/dL | GLU mg/dL |
|----------------|--------------|---------------|--------------|-------------|-------------|-------------|-------------|--------------|
| GROUP: PRETEST | | | | | | | | |
| 18 | 12.5 | 0.41 | 139 | 6.24 | 113 | 10.7 | 10.4 | 127 |
| 45 | 10.6 | 0.37 | 147 | 6.38 | 110 | 11.2 | 12.3 | 132 |
| 48 | 8.0 | 0.43 | 139 | 6.52 | 110 | 11.0 | 11.9 | 125 |
| 56 | 12.7 | 0.36 | 140 | 6.78 | 112 | 11.6 | 12.9 | 161 |
| 75 | 10.9 | 0.45 | 143 | 6.87 | 111 | 12.0 | 12.3 | 192 |
| MEAN | 10.9 | 0.40 | 142 | 6.56 | 111 | 11.3 | 12.0 | 147 |
| SD | 1.89 | 0.038 | 3.4 | 0.265 | 1.3 | 0.51 | 0.94 | 28.8 |
| N | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

PRETEST ANIMAL CLINICAL CHEMISTRY REPORT
PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

| ANIMAL ID | ALT U/L | AST U/L | TP g/dL | ALB g/dL | TBA mg/dL | ALKP U/L | LDH U/L | CK U/L |
|----------------|------------|------------|------------|-------------|--------------|-------------|----------------|-----------|
| GROUP: PRETEST | | | | | | | | |
| 117 | 63 | 131 | 7.1 | 3.8 | 112.8 | 258 | 167 | 544 |
| 143 | 58 | 112 | 7.1 | 4.0 | 123.8 | 261 | 118 | 344 |
| 152 | 61 | 99 | 7.7 | 4.4 | 72.3 | 233 | 54 | 88 |
| 184 | 50 | 120 | 7.9 | 4.4 | 21.7 | 200 | 212 | 181 |
| 197 | 75 | 148 | 6.7 | 4.0 | 301.1 | 257 | 367 | 524 |
| MEAN | 61 | 122 | 7.3 | 4.1 | 126.3 | 242 | 184 | 336 |
| SD | 9.1 | 18.6 | 0.49 | 0.27 | 105.59 | 25.9 | 118.1 | 202.6 |
| N | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |

ml = 25-200

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

PRETEST ANIMAL CLINICAL CHEMISTRY REPORT
PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

| ANIMAL ID | BUN mg/dL | CREA mg/dL | NA mmol/L | K mmol/L | CL mEq/L | CA mg/dL | IP mg/dL | GLU mg/dL |
|----------------|--------------|---------------|--------------|-------------|-------------|-------------|-------------|--------------|
| GROUP: PRETEST | | | | | | | | |
| 117 | 10.0 | 0.49 | 143 | 6.92 | 111 | 11.9 | 11.5 | 175 |
| 143 | 8.9 | 0.42 | 143 | 6.99 | 111 | 12.4 | 10.7 | 150 |
| 152 | 13.6 | 0.40 | 143 | 6.12 | 110 | 11.8 | 10.3 | 138 |
| 184 | 16.9 | 0.45 | 145 | 6.14 | 117 | 12.3 | 10.5 | 129 |
| 197 | 10.9 | 0.45 | 137 | 6.63 | 108 | 11.3 | 10.3 | 133 |
| MEAN | 12.1 | 0.44 | 142 | 6.56 | 111 | 11.9 | 10.7 | 145 |
| SD | 3.22 | 0.034 | 3.0 | 0.415 | 3.4 | 0.44 | 0.50 | 18.5 |
| N | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

PRETEST ANIMAL HEMATOLOGY REPORT
PERIOD: PRETEST

STUDY ID: 098P

SEX: MALE

| ANIMAL ID | RBC 10 ⁶ /cmm | HGB g/dL | HCT % | MCV fL | MCH pg | MCHC g/dL | RETICS %RBCs | HB % |
|----------------|-----------------------------|-------------|----------|-----------|-----------|--------------|-----------------|---------|
| GROUP: PRETEST | | | | | | | | |
| 18 | 6.36 | 14.0 | 41.3 | 64.9 | 22.0 | 33.9 | 3.4 | 0.0 |
| 45 | 6.38 | 13.7 | 40.8 | 63.9 | 21.5 | 33.6 | 1.9 | 0.0 |
| 48 | 6.68 | 14.5 | 42.1 | 63.0 | 21.7 | 34.4 | 3.4 | 0.0 |
| 56 | 6.50 | 16.4 | 42.6 | 65.5 | 25.2 | 38.5 | 2.7 | 0.0 |
| 75 | 6.82 | 15.5 | 44.1 | 64.7 | 22.7 | 35.1 | 2.6 | 0.0 |
| MEAN | 6.55 | 14.8 | 42.2 | 64.4 | 22.6 | 35.1 | 2.8 | 0.0 |
| SD | 0.198 | 1.12 | 1.28 | 0.97 | 1.51 | 1.98 | 0.63 | 0.00 |
| N | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

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PRETEST ANIMAL HEMATOLOGY REPORT
PERIOD: PRETEST

STUDY ID: 098P

SEX: MALE

| ANIMAL ID | PLT 10 ³ /ccm | WBC 10 ³ /cmm |
|-----------|-----------------------------|-----------------------------|
|-----------|-----------------------------|-----------------------------|

GROUP: PRETEST

| | | |
|----|------|------|
| 18 | 1141 | 22.0 |
| 45 | 1075 | 11.4 |
| 48 | 1136 | 13.1 |
| 56 | 1309 | 16.1 |
| 75 | 1396 | 21.6 |

| | | |
|------|-------|------|
| MEAN | 1211 | 16.8 |
| SD | 135.0 | 4.83 |
| N | 5 | 5 |

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

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PRETEST ANIMAL HEMATOLOGY REPORT
PERIOD: PRETEST

STUDY ID: 098P

SEX: MALE

| ANIMAL ID | %METHGB % | APTT sec |
|-----------|--------------|-------------|
|-----------|--------------|-------------|

GROUP: PRETEST

| | | |
|----|-----|------|
| 2 | 0.5 | 11.5 |
| 32 | 1.0 | 10.4 |
| 58 | 0.4 | 8.9 |
| 85 | 0.3 | 10.3 |
| 95 | 0.7 | 16.1 |

| | | |
|------|------|------|
| MEAN | 0.6 | 11.4 |
| SD | 0.28 | 2.76 |
| N | 5 | 5 |

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

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WHITE DIFFERENTIAL DATA

STUDY ID: 098P

GROUP: PRETEST

SEX: MALE

| ANIMAL ID | | PRETEST | |
|-----------|---------------------|---------|------|
| | | REL | ABS |
| 18 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 5 | 1.1 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 92 | 20.2 |
| | Monocytes | 3 | 0.7 |
| | Eosinophils | 0 | 0.0 |
| | Basophils | 0 | 0.0 |
| | WBC | | 22.0 |
| 45 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 6 | 0.7 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 88 | 10.0 |
| | Monocytes | 6 | 0.7 |
| | Eosinophils | 0 | 0.0 |
| | Basophils | 0 | 0.0 |
| | WBC | | 11.4 |
| 48 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 12 | 1.6 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 81 | 10.6 |
| | Monocytes | 5 | 0.7 |
| | Eosinophils | 2 | 0.3 |
| | Basophils | 0 | 0.0 |
| | WBC | | 13.1 |
| 56 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 14 | 2.3 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 77 | 12.4 |
| | Monocytes | 8 | 1.3 |
| | Eosinophils | 1 | 0.2 |
| | Basophils | 0 | 0.0 |
| | WBC | | 16.1 |

NRBC Corrected After-10

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 098P

GROUP: PRETEST

SEX: MALE

| ANIMAL ID | | PRETEST | |
|-----------|---------------------|---------|------|
| | | REL | ABS |
| 75 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 8 | 1.7 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 87 | 18.8 |
| | Monocytes | 4 | 0.9 |
| | Eosinophils | 1 | 0.2 |
| | Basophils | 0 | 0.0 |
| | WBC | | 21.6 |

NRBC Corrected After-10

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098P

SEX: MALE

GROUP: PRETEST

| ANIMAL ID | PRETEST |
|-----------|---|
| 18 | Anisocytosis,Slight; Polychromasia, Moderate;Target Cells,Slight |
| 45 | Polychromasia,Slight Target Cells,Slight; Macrocytes,Slight |
| 48 | Anisocytosis,Slight; Polychromasia,Slight |
| 56 | Polychromasia,Slight Macrocytes,Slight |
| 75 | Anisocytosis,Slight; Polychromasia,Slight Target Cells,Slight |

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

PRETEST ANIMAL HEMATOLOGY REPORT
PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

| ANIMAL ID | RBC 10 ⁶ /cmm | HGB g/dL | HCT % | MCV fL | MCH pg | MCHC g/dL | RETICS %RBCs | HB % |
|----------------|-----------------------------|-------------|----------|-----------|-----------|--------------|-----------------|---------|
| GROUP: PRETEST | | | | | | | | |
| 117 | 7.21 | 15.0 | 43.9 | 60.9 | 20.8 | 34.2 | 2.3 | 0.0 |
| 143 | 6.21 | 13.3 | 38.9 | 62.6 | 21.4 | 34.2 | 0.8 | 0.0 |
| 152 | 6.93 | 14.5 | 41.6 | 60.0 | 20.9 | 34.9 | 1.4 | 0.0 |
| 184 | 6.85 | 14.4 | 41.2 | 60.1 | 21.0 | 35.0 | 2.0 | 0.0 |
| 197 | 6.77 | 14.8 | 42.6 | 62.9 | 21.9 | 34.7 | 2.9 | 0.0 |
| MEAN | 6.79 | 14.4 | 41.6 | 61.3 | 21.2 | 34.6 | 1.9 | 0.0 |
| SD | 0.366 | 0.66 | 1.85 | 1.37 | 0.45 | 0.38 | 0.81 | 0.00 |
| N | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

PRETEST ANIMAL HEMATOLOGY REPORT
PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

| ANIMAL ID | PLT 10 ³ /ccm | WBC 10 ³ /cmm |
|-----------|-----------------------------|-----------------------------|
|-----------|-----------------------------|-----------------------------|

GROUP: PRETEST

| | | |
|-----|------|------|
| 117 | 768 | 12.1 |
| 143 | 1097 | 12.3 |
| 152 | 1049 | 21.5 |
| 184 | 1012 | 15.5 |
| 197 | 1195 | 12.7 |

| | | |
|------|-------|------|
| MEAN | 1024 | 14.8 |
| SD | 158.8 | 3.98 |
| N | 5 | 5 |

WBC corrected for NRBC = or > 10

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

PRETEST ANIMAL HEMATOLOGY REPORT
PERIOD: PRETEST

STUDY ID: 098P

SEX: FEMALE

| ANIMAL ID | %METHGB % | APTT sec |
|-----------|--------------|-------------|
|-----------|--------------|-------------|

GROUP: PRETEST

| | | |
|-----|-----|------|
| 105 | 0.7 | 9.5 |
| 107 | 0.3 | 8.1 |
| 166 | 0.7 | 10.3 |
| 174 | 0.4 | 8.6 |
| 188 | 1.1 | 10.1 |

| | | |
|------|------|------|
| MEAN | 0.6 | 9.3 |
| SD | 0.31 | 0.95 |
| N | 5 | 5 |

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 098P

GROUP: PRETEST

SEX: FEMALE

| ANIMAL ID | | PRETEST | |
|-----------|---------------------|---------|------|
| | | REL | ABS |
| 117 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 7 | 0.8 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 81 | 9.8 |
| | Monocytes | 12 | 1.5 |
| | Eosinophils | 0 | 0.0 |
| | Basophils | 0 | 0.0 |
| | WBC | | 12.1 |
| 143 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 8 | 1.0 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 89 | 10.9 |
| | Monocytes | 3 | 0.4 |
| | Eosinophils | 0 | 0.0 |
| | Basophils | 0 | 0.0 |
| | WBC | | 12.3 |
| 152 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 6 | 1.3 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 92 | 19.8 |
| | Monocytes | 1 | 0.2 |
| | Eosinophils | 1 | 0.2 |
| | Basophils | 0 | 0.0 |
| | WBC | | 21.5 |
| 184 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 16 | 2.5 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 79 | 12.2 |
| | Monocytes | 4 | 0.6 |
| | Eosinophils | 1 | 0.2 |
| | Basophils | 0 | 0.0 |
| | WBC | | 15.5 |

NRBC Corrected After-10

DRAFT

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 098P

GROUP: PRETEST

SEX: FEMALE

ANIMAL ID

PRETEST
REL ABS

| | | | |
|-----|---------------------|----|------|
| 197 | Nucleated Red Cells | 0 | |
| | M. Neutrophils | 16 | 2.0 |
| | I. Neutrophils | 0 | 0.0 |
| | Lymphocytes | 80 | 10.2 |
| | Monocytes | 4 | 0.5 |
| | Eosinophils | 0 | 0.0 |
| | Basophils | 0 | 0.0 |
| | WBC | | 12.7 |

NRBC Corrected After-10

THIRTEEN WEEK ORAL TOXICITY STUDY
OF WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 098P

GROUP: PRETEST

SEX: FEMALE

| ANIMAL ID | PRETEST |
|-----------|--|
| 117 | Anisocytosis,Slight; Polychromasia,Slight Large Platelets, Slight |
| 143 | Polychromasia, Moderate;Macrocytes, Moderate |
| 152 | Anisocytosis,Slight; Polychromasia,Slight |
| 184 | Anisocytosis, Moderate; Polychromasia,Slight |
| 197 | Anisocytosis,Slight; Polychromasia,Slight |

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Appendix 12
Protocol and Protocol Amendments

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR 238605
WITH A THIRTEEN WEEK RECOVERY PERIOD IN RATS

1.0 PURPOSE OF THE STUDY:

The purpose of this study is to determine specific target organ toxicity, dose-response relationships, and a no adverse effect level of WR 238605 in CD® rats following thirteen weeks of daily administration by gavage. In addition, the reversibility of these toxic effects over a 90-day recovery period will be assessed. This study will be conducted in accordance with the specifications of the Sponsor as described in Task Order UIC-5. The protocol for this study was approved by the UIC Animal Care Committee.

2.0 SPONSOR:

2.1 Name: U.S. Army Medical Research
and Development Command

2.2 Address: Fort Detrick
Frederick, MD 21702-5009

2.3 Representative: George Schieferstein, Ph.D.

3.0 TESTING FACILITY:

3.1 Name: Toxicology Research Laboratory (TRL)

3.2 Address: University of Illinois at Chicago (UIC)
Department of Pharmacology
P. O. Box 6998
Chicago, IL 60680

3.3 Study Director: Barry S. Levine, D.Sc., D.A.B.T.

4.0 DATES:

4.1 Study Initiation Date
(see 11.0; Protocol Approval): 9/1/92

4.2 Proposed Initiation of Dosing: 12/17/92

4.3 Proposed Necropsy Dates: 3/18,19/93; 6/17,18/93

4.4 Proposed Study Completion Date
(Draft Study Report): 9/17/93

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5.0 TEST ARTICLE

- 5.1 Name or Code No: WR238605 succinate
- 5.2 TRL Chemical No: 0720614
- 5.3 Physical Description: Pale yellow powder.
- 5.4 Stability and Handling of Test Article:
- 5.4.1 Storage Conditions to Maintain Stability:
- 5.4.1.1 Temperature: 0 - 4°C
- 5.4.1.2 Humidity: Ambient conditions.
- 5.4.1.3 Light: Protect from light: amber bottle or silver foil covering.
- 5.4.1.4 Special Requirements: None.
- 5.4.2 Special Handling Procedures: Standard safety precautions including gloves, eye protection, mask, and lab coats.
- 5.4.3 Log of Test Article: The amount, date, identity of person(s) removing aliquots and the purpose for which each aliquot of the test article was removed from the batch will be documented. At termination of the study, all unused test article will be returned to the Sponsor if requested.

6.0 PERSONNEL:

| | |
|-----------------------|---|
| Study Director | Barry S. Levine, D.Sc., D.A.B.T. |
| Toxicologist | E. Marianna Furedi-Machacek, D.V.M. |
| Pathologist | Michael J. Tomlinson, D.V.M., Ph.D., D.A.C.V.P. |
| Analytical Chemist | Ian R. Tebbett, Ph.D. |
| Clinical Veterinarian | James E. Artwohl, D.V.M., Ph.D., D.A.C.L.A.M. |
| Veterinarian Support | Documented in raw data |
| Ophthalmologist | Samuel J. Vainisi, D.V.M., D.A.C.V.O. |
| Tox. Lab Supervisor | Soudabeh Soura, B.S. |
| Lead Technician | Nancy Dinger, B.S. |
| Clinical Pathology | Maria Lang, A.H.T., C.V.T. |
| Chemistry Specialist | Thomas Tolhurst, B.S. |
| Quality Assurance | Ronald C. Schoenbeck |

7.0 TEST SYSTEM:

- 7.1 Species: Rat
- 7.2 Strain: CD® (Virus Antibody Free)
- 7.3 Number and Sex: 80 Males and 80 Females

DRAFT

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-5B
Study No.: 098

- 7.4 Age of Animals: Approximately 7 weeks old at dosing initiation.
- 7.5 Weight of Animals: Approximately 200 - 250 g (males) and approximately 150 - 200 g (females) at dosing initiation.
- 7.6 Source of Animals: Charles River Breeding Laboratories. The specific breeding facility will be documented in the raw data.
- 7.7 Justification for Selection of Test System: The rat is a standard and accepted rodent species for toxicology studies, and is specified by the Sponsor.
- 7.8 Procedure for Unique Identification of Test System: Upon arrival, each animal will be given a study-unique quarantine/pretest number. During the animal selection process, each animal will be assigned an animal number unique to it within the population making up the study. This number will appear as an ear tag and will also appear on a cage card visible on the front of each cage. The cage card will additionally contain the study number, test article identification, treatment group number and dose level. Cage cards will be color-coded as a function of treatment group. Raw data records and specimens will also be identified by the unique test animal number.
- 7.9 Housing: The animals will be housed in an AAALAC-accredited facility. Animals will be singly housed in polycarbonate cages with Anderson-bed-a-cob bedding (Heinold, Kankakee, Illinois) in a temperature (65-78°F) and humidity (approx. 40-70%) controlled room with a 14 hour light/10 hour dark cycle. The cage size, 840 cm area and 20 cm height, is adequate to house rats at the upper weight range as described in the Guide for the Care and Use of Laboratory Animals, DHEW (NIH) No. 86.23. All animals will be routinely transferred to clean cages with fresh bedding once weekly.
- 7.10 Quarantine Procedure: Animals will be quarantined for approximately one week. During that time, the animals will be observed daily for signs of illness or death, and all unusual observations will be reported to the Study Director, Toxicologist or Clinical Veterinarian. Animals will be examined during quarantine and approved for use by the Clinical Veterinarian prior to being placed on test. Any sickly animals will be eliminated prior to the test animal selection process. If a selected animal appears sickly prior to initiation of treatment, it will be replaced by a healthy animal prior to initiation of treatment under the direction of the Study Director or Toxicologist. In addition, during the quarantine/pretest, hematology and clinical chemistry parameters (see Section 8.7.6) will be measured for five rats/sex to determine the suitability of the rat shipment for use in this study. These rats, however, will not be used in the dosing portion of the study. Quarantine release will be documented on the Clinical Veterinarian Log by the veterinarian prior to study initiation.

DRAFT

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-5B
Study No.: 098

- 7.11 Food: Purina Certified Rodent Chow No. 5002 (Ralston Purina Company, St. Louis, MO) will be provided *ad libitum* from arrival until termination, except during an approximate 16-20 hour fast prior to blood collection for clinical pathology and/or necropsy.
- 7.12 Water: Tap water from an automatic watering system in which the room distribution lines are flushed daily will be provided *ad libitum* from arrival until termination. The water is untreated with additional chlorine or HCl.
- 7.13 There are no known contaminants in the feed or water which are expected to influence the study. A copy of the feed certification will be kept with the study records. The results of bimonthly comprehensive chemical analyses of Chicago water are documented in files maintained by Quality Assurance.

8.0 EXPERIMENTAL DESIGN:

8.1 Treatment Groups:

| <u>Treatment Group</u> | <u>Dose Level (mg base/kg/day)</u> | <u>Number of Males</u> | <u>Number of Females</u> |
|------------------------|------------------------------------|------------------------|--------------------------|
| 1 | 0 | 10 + 10* | 10 + 10* |
| 2 | 0.5 | 10 + 10* | 10 + 10* |
| 3 | 6.0 | 10 + 10* | 10 + 10* |
| 4 | 18.0 | 10 + 10* | 10 + 10* |

*Recovery Animals

Dose levels were supplied by the Sponsor based on the results of a 28-day gavage rat study, and are extrapolations from that shorter-term toxicology study.

Ten animals/sex/group will be necropsied after the thirteen week treatment period. The remaining animals indicated above will be held for a thirteen week recovery period, at which time they will be necropsied.

- 8.2 Frequency and Route of Administration of the Test Article: The test article will be administered by gavage once daily starting with Day 0 for at least thirteen weeks. Control animals will receive the test article vehicle (aqueous 1% methylcellulose/0.4% Tween 80). The animals to be sacrificed after the 13 week treatment period will be dosed up to and including the day prior to their scheduled necropsy on Days 91 and 92. The recovery animals will be dosed for 91 days. Dosing volume will be 5 ml/kg, adjusted on the basis of each animal's most recent body weight. The actual volume (ml) administered will be documented in the raw data.

DRAFT

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-5B
Study No.: 098

- 8.3 Justification of Route(s): Oral treatment is the intended clinical route of administration and is specified by the Sponsor.
- 8.4 Procedure to Control Bias during the Assignment of Animals to Treatment Groups: During the quarantine/pretest period, the animals will be randomized by sex into the four groups shown in Section 8.1 using a computer-generated randomization procedure on the basis of body weight.
- 8.5 Test Article Vehicle: Aqueous 1% methylcellulose/0.4% Tween 80. Both chemicals will be obtained from Sigma. If another source is used, it will be identified in the raw data.
- 8.6 Test Article Dosage Form Preparation and Analyses: The test article dosing suspensions will be prepared every two weeks based on stability data from a previously conducted dog toxicity study by gastric intubation (UIC/TRL Study No. 047). WR 238605 dosage formulations were previously shown to be homogeneous in that study. The test article will be suspended in the vehicle to result in concentrations necessary to administer the dosage formulations at a volume of 5 ml/kg. The specific volume (ml) administered will be calculated on the basis of each animal's most recent body weight. Samples of all dosage formulations used in Weeks 1 & 2, 7 & 8, and 13 will be analyzed for test article concentration prior to their use. Only samples within 10% of their target concentration will be used.
- 8.7 Type and Frequency of Observations, Tests, Analyses and Measurements:
- 8.7.1 Clinical Signs: All animals will be observed once daily for clinical signs of toxicity approximately 1 - 2 hours after dosing. Additionally, all animals will be observed for moribundity/mortality in the afternoon and immediately prior to dosing in the morning. During the recovery period, clinical signs will be recorded in the morning.
- 8.7.2 Clinical Observations: All animals will be subjected to a physical examination including examination of eyes and all orifices in Week -1, on Day 0, and weekly thereafter.
- 8.7.3 Body Weight: Body weights of all animals will be recorded at randomization in Week -1, on Day 0, weekly thereafter, and at scheduled necropsy.
- 8.7.4 Food Consumption: Food consumption for all animals will be measured weekly commencing in Week -1.
- 8.7.5 Ophthalmologic Examinations: All rats will be examined by indirect ophthalmoscopy prior to study initiation and during Week 13, and in Week 26 for the recovery animals.

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- 8.7.6 Clinical Pathology: Hematology and clinical chemistry parameters will be measured for 10 animals/sex/group during Weeks 2, 4, 8 and 13, and in Weeks 16, 21 and 27 (at necropsy) for the recovery groups. The recovery animals will be routinely used throughout the study for these measurements. The overnight fasted animals will be anesthetized by carbon dioxide inhalation, and approximately 1.5 - 2.0 ml of blood will be collected from the orbital sinus to measure the following parameters. The samples will be processed in the same random order as collected.

Hematology

| | |
|---|---|
| ^a Erythrocyte count and morphology | Mean cell volume(MCV) |
| Hematocrit | Mean cell hemoglobin (MCH) |
| Hemoglobin | Mean cell hemoglobin concentration (MCHC) |
| Leukocyte count, total and differential | Heinz Bodies |
| Reticulocyte counts | Platelet count |
| | ^b Methemoglobin |

^a Includes nucleated RBCs.

^b To be measured with a Co-oximeter (Instrumentation Laboratory Model No. 282). The assay will be performed within one hour of sample collection. The specimens will be kept on wet ice prior to analysis.

Clinical Chemistry

| | |
|---------------------------------------|-----------------------|
| Albumin | Creatine kinase |
| Albumin/Globulin Ratio (calculated) | Chloride |
| Alkaline phosphatase | Glucose |
| Alanine aminotransferase (ALT/SGPT) | Globulin (calculated) |
| Aspartate aminotransferase (AST/SGOT) | Inorganic phosphorus |
| Calcium | Lactate dehydrogenase |
| Creatinine | Potassium |
| | Sodium |
| | Total bile acids |
| | Total protein |
| | Urea nitrogen (BUN) |

Activated partial thromboplastin time will be measured for all rats from blood samples collected from the vena cava at their scheduled necropsy in Weeks 14 and 27. Clinical chemistry and hematology tests and activated partial thromboplastin time will be measured for 5 rats/sex during the quarantine/pretest period.

- 8.7.7 Plasma Drug Levels: Blood samples will be obtained at scheduled necropsy from the vena cava to provide approximately 1 ml of plasma for drug level measurements. The samples will be collected after blood is obtained for activated partial thromboplastin time. The plasma samples will subsequently be shipped to Dr. Emil Lin for analysis as specified by the Sponsor. The results will not be included in the Study Report.

DRAFT

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-5B
Study No.: 098

8.7.8

Pathology: All animals which die on test or are sacrificed if moribund will be necropsied on that day. For surviving animals, 10 animals/sex/group will be sacrificed and necropsied in random order over two consecutive days (Days 91 and 92). The remaining animals will be held for a 13 week recovery period. They will be sacrificed and necropsied at the onset of Week 27.

Euthanasia will be accomplished by carbon dioxide asphyxiation, and an extensive necropsy will be performed under the direction and supervision of the pathologist. Terminal body weights will be collected prior to routine sacrifice.

The necropsy procedure will be a thorough and systematic examination and dissection of the animal viscera and carcass, and collection and fixation of the following tissues/organs in 10% neutral buffered formalin.

| | |
|----------------------------|---------------------------------|
| *Adrenal glands | *Ovaries |
| Animal identification | Pancreas |
| *Brain | Pituitary |
| Cecum | Prostate |
| Colon | Rib with costochondral junction |
| Diaphragm | Salivary gland (submaxillary) |
| Duodenum | Sciatic nerve |
| Esophagus | Skeletal muscle |
| Eyes with harderian glands | Skin with mammary gland |
| Femoral marrow smear | Spinal cord (thoracic) |
| *Heart | *Spleen |
| Gross lesions | Sternum with marrow |
| Ileum | Stomach |
| Jejunum | *Testes with epididymides |
| *Kidneys | Thymus |
| *Liver | Thyroid gland/Parathyroids |
| Lungs/Bronchi | Tongue |
| Lymph node (mesenteric) | Trachea |
| | Urinary bladder |
| | Uterus |

*Weighed at scheduled necropsy. Paired organs will be weighed as a unit.

All tissues and organs collected at necropsy will be examined microscopically for all high dose and control animals sacrificed after 13 weeks of treatment. In addition, animals found dead or subjected to a moribund sacrifice will also be processed for microscopic examination. If treatment-related lesions are observed at the high dose, those tissues/organs will be examined microscopically for mid and low dose animals sacrificed in Week 14, and for control and high dose (and mid and low dose if necessary) recovery animals.

DRAFT

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-5B
Study No.: 098

Femoral bone marrow smears will be prepared for all animals at scheduled necropsy and for moribund sacrificed animals. The myeloid:erythroid (M:E) ratio will be determined for control and high dose animals at the Week 14 necropsy. If treatment-related changes are seen, M:E ratios will be determined from mid and low dose animals at Week 14, and from control and high dose (and mid and low dose as necessary) recovery animals.

8.7.9 Statistical Analyses: For each sex, Analysis of Variance tests will be conducted on body weight, food consumption, hematology, clinical chemistry and organ weight data. Organ weight analysis will consider absolute weights and weights relative to body weight. If a significant F ratio is obtained ($p \leq 0.05$), Dunnett's t test will be used for pair-wise comparisons to the control group. Frequency data such as incidence of mortality, gross necropsy observations and tissues morphology observations will be compared by Fishers Exact Test or Chi-square analyses as necessary.

Quantitative data will be tabulated and presented in the report. In addition to the written report, summary data tables of parameters and variability will be transmitted to the Sponsor on magnetic media (computer diskette) in "ASCII" form. The transcribed data on disk will no longer be considered GLP compliant.

9.0 RECORDS TO BE MAINTAINED:

All data generated during the conduct study, except those that are generated as direct computer input, shall be recorded directly, promptly, and accurately in ink in bound books with prenumbered pages or on worksheets that shall be bound during or at the conclusion of the nonclinical laboratory study. All appropriate computer and machine output shall be bound during or at the conclusion of the study. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data. Any changes in entries for whatever reason (e.g., to correct an error or transposition) shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of data input. In computer driven collection systems, the operator responsible for direct input shall be identified at the time of data input. Any changes in computer entries for whatever reason (e.g., to correct an error or transposition) shall be made in such manner so as not to obscure the original entry, if possible, shall indicate the reason for such change, and shall be dated and the responsible individual shall be identified.

All recorded data shall be reviewed, signed, and dated by a knowledgeable person, other than the person making the entry, to assure adherence to procedures and to verify observations.

Upon completion of the study and submission of the final report, all raw data, documentation, specimens, test article reserves and other materials necessary to reconstruct the study will be stored in the TRL archives

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Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-58
Study No.: 098

maintained by Quality Assurance, unless specified by the Sponsor.

All changes or revisions, and reasons therefore, to this protocol once it is approved shall be documented, signed by the Study Director and Sponsor, dated and maintained with the protocol.

10.0 REGULATORY REQUIREMENTS:

This study will be performed in compliance with the UIC/TRL Quality Assurance Program designed to conform with FDA Good Laboratory Practice Regulations and EPA Good Laboratory Practice Standards.

Will this study be submitted to a regulatory agency? Yes

If so, to which agency(ies)? Food and Drug Administration

Does the Sponsor request that test article samples be returned? Yes

Does the Sponsor request that samples of the test article/carrier mixture(s) be returned? No

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Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-5B
Study No.: 098

11.0 PROTOCOL APPROVAL:

STUDY DIRECTOR:

Barry S. Levine
Barry S. Levine, D.Sc., D.A.B.T.

9/1/92
Date

QUALITY ASSURANCE:

Ronald Schöenbeck
Ronald Schöenbeck

9/1/92
Date

SPONSOR APPROVAL:

George Schieferstein
George Schieferstein, Ph.D.
Contracting Officer's
Representative (COR)

9/2/92
Date

COMMENTS FROM THE COR:

PROTOCOL AMENDMENT

DRAFT

Study No.: 098

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats

1. Page 1 Section 4.0

Change the study dates as follows:

4.2 Proposed Initiation of Dosing: 12/17/92

4.3 Proposed Necropsy Date: 3/18,19/93; 6/17,18/93

4.4 Proposed Study Completion Date
(Draft Study Report): 9/17/93

Reason: Delay in study start.

2. Page 2 Section 6.0

Change "Technician Teresa O'Neill, B.S." to "Lead Technician Nancy Dinger, B.S."

Reason: Mistake in protocol.

3. Page 6 Section 8.7.6

A. Change the blood collection weekly timepoints for clinical pathology measurements from "3, 5, 9, 13, 16, 18, 22 and 27" to "2, 4, 8, 13, 16, 21 and 27."

Reason: Sponsor request.

B. Add total bile acids (TBA) to the clinical chemistry list.

Reason: Inadvertently omitted from protocol.

C. Change "abdominal aorta" to "vena cava" in the last sentence which describes the collection of blood for activated partial thromboplastin time.

Reason: Mistake in protocol.

D. Add the following sentence at the end of the section:

"Clinical chemistry and hematology tests and activated partial thromboplastin time will be measured for 5 rats/sex during the quarantine/pretest period."

PROTOCOL AMENDMENT

DRAFT

Study No.: 098

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats

Reason: Clarification of procedures.

4. Page 6 Section 8.7.7

Change "abdominal aorta" to "vena cava" as the source of blood collection in the first sentence.

Reason: Mistake in protocol.

5. Page 7 Section 8.7.8

Add "sternum with marrow" to the tissue list.

Reason: Inadvertently omitted from the protocol.

6. Page 8 Section 8.7.8

Change the first sentence as follows:

"Femoral bone marrow smears will be prepared for all animals at scheduled necropsy and for moribund sacrificed animals."

Reason: Clarification of protocol.

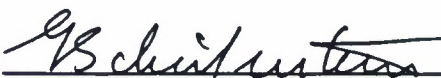
APPROVALS:

STUDY DIRECTOR:


Barry S. Levine, D.Sc., D.A.B.T.

12/21/92
Date

SPONSOR APPROVAL:


George Schieferstein, Ph.D.
Contracting Officer's
Representative (COR)

12/23/92
Date

PROTOCOL AMENDMENT

DRAFT

Study No.: 098

Title: Thirteen Week Oral Toxicity Study of WR238605 with a Thirteen Week Recovery Period in Rats

7. Page 2 Section 5.3

Change "White powder" to "Pale yellow powder"

Reason: Mistake in the protocol

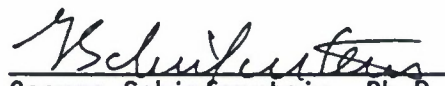
APPROVALS:

STUDY DIRECTOR:


Barry S. Levine, D.Sc., D.A.B.T.

5/5/93
Date

SPONSOR APPROVAL:


George Schieferstein, Ph.D.
Contracting Officer's
Representative (COR)

5/2/93
Date

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Appendix 13
Study Deviations

THIRTEEN WEEK ORAL TOXICITY STUDY OF
WR238605 WITH A THIRTEEN WEEK
RECOVERY PERIOD IN RATS

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Study Deviations*

| <u>Deviation Type</u> | <u>Specific Deviation</u> | <u>Effect on Study</u> |
|-----------------------|---|---|
| Protocol | On several occasions the temperature deviated outside the specified range in the animal room(s.) The temperature deviations ranged from -0 to +3°F, outside the specified ranges. | None. These minimal sporadic occurrences were not considered to have had an impact on the outcome of the study. |
| Protocol | In an attempt to identify unknown pigment (hemosiderin or lipofuscin) present in the alveolar macrophages in the lungs of recovery rats, Perl's and acid-fast staining of lung sections were performed. | These stains allowed the identification of pigment as hemosiderin. |

*The detailed "Deviation Reports" are contained in the raw data which are archive at the University of Illinois at Chicago, Department of Pharmacology, Chicago, Illinois.

The above deviations did not affect the integrity of the study.

Barry S. Levine, D.Sc., D.A.B.T.

Date